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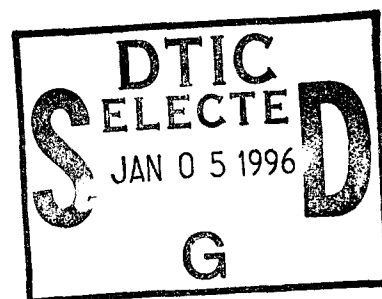
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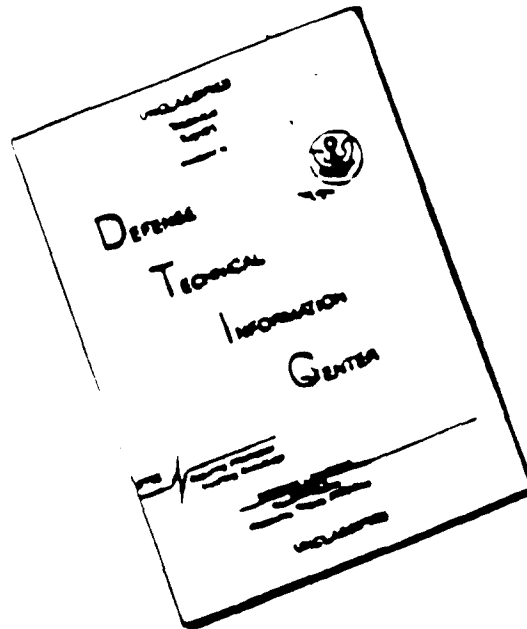
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Mary B. Daly 10/13/95
PI - Signature Date

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Introduction

A. Nature of the Problem

Breast cancer is the most prevalent cause of cancer in women in the United States and the second leading cause of death due to cancer. It is estimated that in 1995 approximately 183,400 individuals will be diagnosed with breast cancer, and 46,240 will die from the disease (1). Age-adjusted incidence rates for breast cancer have risen 30.1% over the past 15 years (2). Mortality rates, however, have remained constant, resulting in a continually escalating burden of breast cancer morbidity and mortality. Not all women share the same risk for breast cancer. Geographical analyses have shown that there is an alarming increase in breast cancer incidence and mortality rates among women residing in the northeastern and mid-Atlantic states compared to other regions (3). A number of specific risk factors, both endocrinologic and environmental, have been shown to confer modest elevations in risk. Breast cancer is predominantly a disease of older age with incidence rates rising linearly with increasing age. When it is diagnosed among young, pre-menopausal women however, it has a more aggressive clinical course and a higher case-fatality rate (4). Significant geographic and ethnic variations in rates have been observed. Rates are highest for white women in the industrialized countries of northern and western Europe and North America, and lowest in Japan. Although African American women have historically had an overall lower risk of developing breast cancer than white women, this difference has narrowed. Since 1969, a black/white cross-over in age-specific breast cancer rates has been observed: among women under age 40, the incidence rate has become higher among black compared with white women, while among women over age 40, the rate has remained higher among white women. Furthermore, the average annual age-adjusted mortality rate per 100,000 is higher in black (30.3) than in white women (27.4) (5).

There is a large body of data supporting a role for reproductive hormones in the development of breast cancer. Nulliparity, early age at menarche, late age at menopause, and late age at first full-term pregnancy have long been associated with an increased risk. More recently, multiparity and lactation have been shown to alter risk independently of other reproductive factors (6). Very preliminary data now suggest an increased risk associated with induced abortion, particularly among women at the extremes of reproductive age (less than 18 and older than 30 years) (7). Further support for a crucial role for estrogen in the development of breast cancer comes from the observed increase in risk associated with prolonged post-menopausal estrogen replacement therapy, and with post-menopause onset obesity, which enhances the production of endogenous estrogen (8). A series of elegant experiments have elucidated the role of endogenous and exogenous hormones in the expression of mammary carcinoma in a rodent model, and have laid the foundation for further exploration of the molecular basis of hormonal effects on human breast cancer (9). Finally, a series of environmental exposures, including radiation, (especially during childhood), alcohol, dietary fat, and pesticide residues have also been suggested as significant risk factors for breast cancer (10-13).

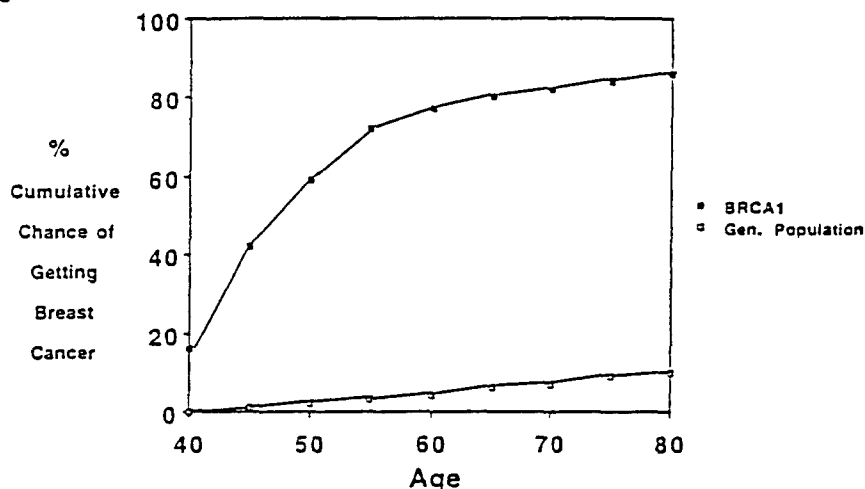
From these observations a complex picture of breast carcinogenesis emerges in which biologic profiles of the host interact with environmental exposures to initiate and promote malignant transformation. Our ability to fully understand these processes in a way that can lead to primary prevention will be enhanced by a better understanding of the molecular events which accompany this process. Recent progress in the molecular genetics of cancer offers new hope of expanding our knowledge and narrowing the gap between epidemiologic data and basic science.

Among the factors associated with breast cancer, none, other than gender and age, alters the magnitude of risk more than a family history of the disease. The increased risk for

both initial and contralateral disease associated with a family history of breast cancer is approximately two- to four-fold (14). The genetics of breast cancer appears to be extremely complex and heterogeneous, with at least three types of familial aggregation observed: 1) families in whom sporadic cases cluster incidentally; 2) families in whom one or more inherited susceptibility profiles enhance the possibility of malignant transformation; and 3) families with truly hereditary breast cancer in whom an autosomal dominant cancer susceptibility gene with high penetrance is inherited. This latter group, in whom the risk of developing breast cancer may approach 85% among mutation carriers (15), may comprise 5 - 10% of all breast cancer. Hereditary breast cancer is characterized by heterogeneity of age at onset, bilaterality, vertical transmission through either parent, and association with tumors of other organs, particularly the ovary, colon and endometrium (16,17).

In 1990, a susceptibility gene for breast cancer was mapped by genetic linkage to the long arm of chromosome 17, in the interval 17q12-21 (18). The linkage between breast cancer and genetic markers on chromosome 17q was soon confirmed by others, and evidence for the coincident transmission of both breast and ovarian cancer susceptibility in linked families was observed (16). This susceptibility gene, which has become known as BRCA1, appears to be responsible for disease in 45% of families with multiple cases of breast cancer only, and up to 90% of families with both breast and ovarian cancer (19). In these families, the cumulative risk for breast cancer in women with a mutant BRCA1 gene is estimated to be 73% by age 50 and 87% by age 70 (Figure 1) (15). There is also preliminary evidence that carriers of the mutant BRCA1 gene may also be at risk for colon and prostate cancer (20).

Figure 1. Cumulative Incidence of Breast Cancer in BRCA1 carriers



The BRCA1 gene has recently been definitely identified by positional cloning methods and has been found to encode a protein of 1863 amino acids. To date, a total of 80 mutations of BRCA1 have been identified in DNA samples from women with familial and sporadic breast and/or ovarian cancer, the majority of which are frameshift or nonsense mutations (21). These mutations are likely to result in missing or non-functional proteins, supporting speculation that BRCA1 is a tumor suppressor gene (22). The frequency of mutations in BRCA1 is thought to be as high as 1 in 300 in the general population (23). Furthermore, new evidence suggests that the prevalence of specific BRCA1 mutations may be as high as 1 in 100 among Ashkenazi Jews (24). A second breast cancer susceptibility gene, BRCA2, has been localized to the long arm of chromosome 13 and appears to confer a high risk of predominantly early-onset breast cancer and may account for some hereditary cases of male breast cancer (25). Finally, linkage analysis in families with both breast and ovarian cancer suggests a third susceptibility gene on chromosome 17q, distal to the BRCA1 gene. Also a tumor suppressor gene, this mutation has been observed in tumors from both sporadic as well

as familial cases, suggesting that it may be either inherited as a germ line mutation or acquired in breast or ovarian tissue during a woman's lifetime (26). Breast cancer is also a component of the rare Li-Fraumeni syndrome in which germ line mutations of the p53 gene on chromosome 17q have been documented (27). The identification and location of these breast cancer genes will now permit further investigation of the precise role they play in cancer progression and will allow us to determine the percentage of total breast cancer caused by the inheritance of mutant genes. This in turn will ultimately enrich our understanding of all breast cancer, sporadic as well as hereditary, and will facilitate the identification of high risk individuals.

A large computerized data base which includes both genetic and environmental risk information from a racially and ethnically diverse set of patients with familial breast cancer, and from women at increased risk for the disease due to a positive family history, will allow investigators from a wide range of disciplines to address questions of gene-environment interactions, of the relative role of reproductive events in women with a genetic risk for breast cancer, and of the underlying reasons for differences in morbidity and mortality from breast cancer in different age and racial groups. It will further our understanding of the genetic basis of breast cancer by identifying families appropriate for genetic studies. The opportunity to maintain long-term follow-up of the women enrolled in the registry will permit evaluation of the effectiveness of new surveillance and prevention strategies.

B. Background of Previous Work

The Family Risk Assessment Program (FRAP) was established at FCCC in 1991 by Dr. Daly to meet several needs: 1) to offer to breast cancer patients and their family members education and information about cancer risk, screening, diagnosis, and treatment; 2) to serve as a research base for ongoing evaluation of the epidemiologic, biologic, genetic and environmental lifestyle factors which influence breast cancer risk; 3) to develop predictive models which will incorporate pedigree data, linkage analysis information and epidemiologic risk factors to more precisely estimate cancer risk; and 4) to develop models for the communication of breast cancer risk information.

Candidates for FRAP include women with one or more first degree relative with breast and/or ovarian cancer. They are identified through their affected relatives, or are self-referred or referred by their primary care physicians for cancer risk counseling. Since the inception of the program a total of 670 high risk women have become participants in the program. Their ages range from 21 years to 75 years, with a median of 40 years. The majority (97%) of the participants are Caucasian, while 3% are African American, Hispanic, or Asian.

On the basis of data provided by each participant on both family history and other pertinent risk factors, an individualized risk estimate for breast cancer is calculated. Trained counselors consider not only the occurrence of cancer within the family, but also the patterns of occurrence and the ages of the affected individuals in determining the type of familial pattern observed. Approximately 40% of FRAP participants meet the criteria for putative hereditary breast/ovarian cancer (i.e. three or more affected relatives in two or more generations) (28), and are eligible for genetic testing protocols. Genetic testing is done in collaboration with Dr. Andrew Godwin.

To date, we have collected more than 100 families with clustering of cancers, that include primary breast and/or ovarian cancers, through the FRAP at FCCC. We have identified germ-line mutations within these families in the *BRCA1*, *CDKN2/MLM*, *TP53*, and *OVCA1* genes. A sampling of our results is presented.

Forty-seven unrelated individuals, affected with breast and/or ovarian cancer and having one or more first degree relatives with either ovarian cancer (any age) or breast cancer (<50 yrs), were screened by SSCP analysis for germ-line mutations in the three regions of *BRCA1* that are most frequently altered (21). Ten mutations were detected, seven in exon 2 and three in exon 11, including one novel mutation. Nine of these mutations presumably result in a frameshift and premature termination of translation. Additional lymphocyte DNAs were available for a number of other affected or at-risk individuals. Using SSCP, these research participants were evaluated for mutant allele carrier status. An example of SSCP analysis results for one family is shown in **Figure 2 (see Addendum A)**. In some cases, it is difficult to distinguish between benign polymorphisms and pathological mutations. In **Figure 3 (see Addendum A)** for example, kindred 83 possesses a missense mutation at nucleotide position 4158. This substitution of an A to G in codon 1347 changes an Arg to a Gly. This same nonconserved amino acid substitution is inherited both maternally and paternally and does not completely segregate with disease. Furthermore, the proband's mother and father, both with additional family histories of disease (not shown), did not share the same haplotype for the mutant *BRCA1* allele indicating that her parents are not distantly related. This alteration was not detected in more than 100 control and 200 at-increased-risk chromosomes. Thus, it is not clear whether these sequence changes represent a mutation with low penetrance and that the early-onset ovarian cancer was sporadic or that the change represents a very rare polymorphism. Two other groups have identified this missense mutation in two unrelated cancer-prone kindreds, but not in large panels of control chromosomes. In one of these cases, however, the variant was found in a patient who also had a frameshift mutation, bringing into question its functional significance (21). These results suggest that even by screening cases and controls, some rare polymorphisms may be mistakenly identified as predisposing mutations or that some missense mutations will be overlooked as pathologically important, if adequate control samples representing appropriate ethnic backgrounds are not available. These results emphasize a need to ultimately determine the biological function of each variant protein. Furthermore, we have identified a novel frameshift mutation, 4153delA, in Family 164 that also does not segregate with disease, indicating the occurrence of a sporadic case of breast cancer or that a second predisposing mutation is inherited maternally.

Current criteria set for screening individuals at high risk for breast and/or ovarian cancer may exclude certain families from genetic testing. For example, a mutation in *BRCA1* was detected in an asymptomatic individual who had one first degree relative that developed late-onset breast cancer. An additional 38 unaffected individuals with a limited family history of disease (one first degree relative with breast and/or ovarian cancer at any age and no more than one affected second degree relative with breast and/or ovarian cancer at age >50 yrs) were screened for mutations. Three frameshift mutations and a novel 2bp insertion in intron 1 were detected. Interestingly, this 2bp insertion is near the 3'-splice acceptor site and may result in an aberrant transcript. Studies are underway to determine the effect of this insertion on RNA splicing.

We also evaluated fifteen individuals affected with breast and/or ovarian cancer and one individual affected with endometrial cancer, all who reported being of Ashkenazi Jewish heritage, for germ-line mutations in exon 2. Five of the fifteen individuals with breast and/or ovarian cancer (33%) and the individual with endometrial cancer (100%) possessed a germ-line mutation; three with the 185delAG and three with the 188del11 frameshift mutation. Review of the family histories of the three 185delAG mutant allele carriers indicated a strong history of breast and ovarian cancer for only JW44. JW80 developed early onset breast cancer, but had only one other relative with cancer (i.e., a mother with ovarian cancer diagnosed at age 55 yrs). The other mutant allele carrier, UPN 231 was diagnosed with both breast cancer (age 50 yrs) and ovarian cancer (age 54 yrs). UPN 193 was also selected based on her Jewish ancestry. Interestingly, this individual was diagnosed with endometrial cancer

at age 81, a tumor type not commonly associated with the breast/ovarian cancer syndrome, yet she possessed a severe *BRCA1* frameshift mutation (i.e., 188del11). Evaluation of DNA from a portion of the tumor revealed that it was homozygous for the mutant allele, indicating a potential causal role in tumor development. Another late onset cancer was found associated with the 188del11 mutation. UPN 253, a Jewish female was diagnosed with a grade III infiltrating ductal carcinoma (IDC) of the breast at age 87 yrs. She, too, has a limited family history of breast and ovarian cancer (i.e., a sister with breast cancer, a niece with Wilm's tumor, and an uncle with pancreatic cancer) as does UPN 261 (i.e., a maternal grandmother with breast cancer at age 50). Four additional frameshift mutations (a 185delAG and three 188del11) were detected in two individuals affected with breast cancer and two women affected with ovarian cancer, when 104 additional cancer patients, unselected for ethnicity and family history, were analyzed for mutations in exon 2. UPN 259 is an African American female diagnosed with IDC of the breast at age 75 yrs. She reported a maternal history of breast cancer, however the number and age of onset of these cancers has not been verified. In comparison, UPN 262 is a female (race not reported) who developed breast cancer at 49 yrs of age. She reported no history of breast or ovarian cancer, however her father was diagnosed with late-onset (>60 yrs) prostate cancer. Interestingly, five of the seven 188del11 mutant allele carriers that we have identified are of Jewish descent. Studies are underway to determine if these five individuals identified in our study share a common haplotype (for the D17S855, D17S1322, D17S1323, and D17S1327 polymorphisms) and whether this mutation may be common to a subset of Ashkenazi Jews.

Given the heterogeneity in breast-ovarian cancer families, correlation of a phenotype such as a higher risk of ovarian cancer with a given mutation would be very helpful in counseling mutant allele carriers. While few such correlations between *BRCA1* genotype and phenotype are so far obvious, we have observed that families with the 185delAG mutation may have a higher incidence of ovarian cancer 41% (23 ovarian cancers of 56 total breast and ovarian cancers) as compare to the reported incidences associated with the 4184del4 (21%; 7 of 34) and the 5382insC (26%; 16 of 61) mutations (21, 29). However, many more families carrying these and other mutations in *BRCA1* are necessary to clearly demonstrate such a trend. Overall, our results suggest that current screening criteria may be too restrictive and may miss a significant portion of individuals at increased risk of developing disease and that ethnic subgrouping may provide a potential short-cut to identify *BRCA1* mutant allele carriers.

As an integral part of cancer risk assessment and counseling, screening guidelines are tailored for high risk individuals and opportunities for primary prevention, such as lifestyle changes, avoidance of carcinogen exposure, or chemoprevention trials are incorporated into the program. The FRAP program has been responsible for the identification and recruitment of eligible candidates for the NSABP BCPT, and currently monitors a total of 238 women participating in the trial. One hundred eighty-five women with a family history of ovarian cancer are enrolled in a screening study to determine the efficacy of the combination of pelvic exam, CA-125 and transvaginal ultrasound with Color Flow Doppler in detecting early stage ovarian cancer. FRAP participants are also involved in a series of pilot studies to further elucidate hormonal and dietary risk profiles and to test novel opportunities for preventive intervention among high risk women (30).

Our interest in and experience with the behavior components of the counseling process has led to the design of a series of research programs which build upon a cognitive-affective theoretical model of information processing to predict how women will respond to risk information. In collaboration with Drs. Caryn Lerman and Barbara Rimer, we are evaluating the impact of a standardized protocol for individualized breast cancer risk counseling on comprehension of personal risk among first-degree relatives of index breast cancer patients. At baseline we found a significant disparity between levels of risk perception and screening adherence and objective risk factors, suggesting that demographic and/or psychosocial

variables may be more salient to risk comprehension and risk-related behavior (31). A preliminary follow-up analysis has shown that women who received risk counseling were significantly more likely to improve their risk comprehension, compared with women in the control situation. African American women, who comprised 10% of the study population, were more likely to benefit than white women. However, the risk counseling did not improve risk comprehension outcomes among those women exhibiting high levels of anxiety related to breast cancer at baseline, indicating that in addition to information about risk, attention to breast cancer worries must also be addressed in the counseling setting (32). These findings highlight the need to include women who bring different cultural and psychosocial expectations to the counseling experience in these trials.

C. Purpose of the Present Work

The establishment of a registry of high risk families is an ideal way to further our understanding of the mechanisms of breast carcinogenesis, and to learn the best ways to provide information and counsel both to women at increased risk for breast cancer and to their primary care practitioners. A large computerized data base which includes both genetic and environmental risk information from a racially and ethnically diverse population will allow investigators to address questions of gene-environment interactions, of the relative role of reproductive events in women with a genetic risk for breast cancer, and of the underlying reasons for differences in morbidity and mortality from breast cancer in different age and racial groups. It will further our understanding of the genetic basis of breast cancer by identifying families appropriate for linkage analysis studies. The inclusion of a High Risk Specimen Bank in the design of this registry will allow investigators to identify and quantify early premalignant markers of breast cancer risk and to estimate the true prevalence of breast cancer gene(s) in the population. Despite widespread public interest in breast cancer, many first degree relatives of breast cancer patients know very little about their true risk status. The establishment of this registry will give us the opportunity to test different counseling strategies so that we can best meet the needs and demands for information which will accompany the eventual identification of breast cancer susceptibility genes. Long-term follow-up of women enrolled in the registry will permit evaluation of the effectiveness of surveillance and prevention strategies. Finally this registry will serve as a catalyst for the development of educational materials directed towards community-based health care professionals. In the past, genetics counseling has been the exclusive domain of medical geneticists and medical genetics counselors. However, to be successful, the transfer of information generated by the Human Genome Project to the public health realm of cancer control must be put in the hands of the primary care practitioner, both physician and nurse. Essential to the successful development of a community-base Breast Cancer Risk Registry is the ability of primary care practitioners to target breast cancer screening and prophylaxis towards truly high risk individuals, and the dissemination of genetic information back to the primary health care team in the community. The educational tools developed to complement the establishment of a high risk registry will serve as a model for bringing primary care practitioners to the forefront of cancer control and prevention.

D. Methods of the Approach

The methods of accomplishing the proposed goals were set out in the grant proposal in eight specific aims. The first step proposed was the establishment of a Breast Cancer Risk Advisory Board representing health care professionals, both at FCCC and the Fox Chase Network, community representatives, as well as lay consumers. This group would have the mandate to provide information, counsel and advice to the staff of the Breast Cancer Risk Registry regarding the legal, social and ethical implications of the new genetic knowledge emerging from the Human Genome Project.

Interaction with the Network hospitals would begin with the development of a plan of recruitment for first degree relatives of women with breast cancer in collaboration with the Medical Director of each Network Oncology Program.

The data management system for the FCCC Family Risk Assessment Program, which uses the relational data base product Oracle as the primary software platform for data entry and validation, storage, retrieval, modification, and security, was proposed as the model for the Network system. The expansion of this data system to a Network-wide Breast Cancer Risk Registry, in addition to maintaining all data in an accurate and consistent fashion, would accommodate the initial distribution of mailed self report questionnaires, and generate appropriate introduction letters, as well as feedback letters for both the participant and her primary care physician. It would also be capable of generating multigenerational pedigrees summarizing the family history, for use both as an educational tool and also to identify those families appropriate for more intensive genetic investigation.

The protocols to be developed for selection of individuals and families for closer genetic investigation and counseling, would include informed consent documents appropriate for the various stages of genetic testing in language amenable to the lay person. Essential to the success of the Registry is the development of programs to train both nurses and physicians at each Network hospital for their expanded role in cancer risk identification and counseling.

Protocols currently being used at FCCC for the collection, transportation and processing of blood samples for genetic testing were proposed as the model for the Network Hospitals. Dr. Jose Russo, Director of Experimental Pathology at FCCC, agreed to guide the expansion of a High Risk Breast Specimen Bank.

Quality control measures would be established to ensure that OSHA standards for the handling of human biologic materials will be followed by all specimen bank and laboratory personnel.

A preliminary survey of all primary care practitioners who treat adults and who are affiliated with the Network hospitals would assess: 1) current practices regarding the identification of cancer prone individuals; 2) attitudes towards cancer screening among high risk individuals; 3) willingness to assume a primary role in cancer risk counseling; and 4) information and support needs to facilitate participation in a high risk registry. The information obtained from the survey, would then be used to build upon the educational resources available through the FCCC Network system (see **Table I**). The establishment and maintenance of contact with each physician who provides primary care for registry members, to inform them of their patient's participation, and to introduce them to the educational resources dealing with cancer genetics available to them through the Network system, is a high priority.

Table I. Fox Chase Network

| | Mamm- ography | Diet and Nutr. Prog. | Family Support Groups | Women's Center | Br Ca Risk Prog. | BSE Training |
|-------------------|------------------|-------------------------|--------------------------|-------------------|---------------------|-----------------|
| St. Luke's | X | X | X | X | | X |
| Reading | X | X | X | | | |
| PolyClinic | X | X | X | | X | |
| Burlington (Mem.) | X | X | X | X | X | X |
| St. Francis | X | X | X | X | X | X |
| Montgomery | X | X | X | X | X | X |
| North Penn | X | X | X | | | |
| St. Mary's | X | X | X | | | X |
| Paoli | X | X | X | | X | X |
| Riverview | X | X | X | X | X | X |
| Hunterdon | X | X | X | | | X |
| Delaware County | X | X | X | | X | X |
| South Jersey | X | X | X | | | X |
| Community Med. | X | X | X | X | | X |

The development of the FCCC Network Breast Cancer Risk Registry will provide the opportunity to develop and evaluate educational and psychological strategies to optimize breast cancer risk counseling in the community setting. Plans to seek additional funding to study and identify the optimal way of delivering breast cancer risk information, the best way to provide this information, and the true impact of counseling programs on participants' risk comprehension, psychological adaptation, and adoption of recommended health practices, have been formulated.

Body

The fundamental premise for the tasks of Year One was that a basic understanding of the current cancer control programs and the unique needs of each Network institution were essential to program implementation. Therefore, the overall goal for this task was to assess the administrative and education needs of the Network hospitals in order to provide a foundation for the entire program implementation process. The following describes the developmental process and the tasks that have been accomplished in Year One.

A. Development of the Breast Cancer Risk Registry Molecular Genetics Testing Facility

Protocols and procedures for genetic testing of Registry participants have been modeled on those established for the FCCC Family Risk Assessment Program. This Genetics Testing Facility will provide a series of molecular/genetic tests designed to identify germ-line mutations in a series of breast/ovarian cancer susceptibility genes. Registry participants meeting at least one of the family selection criteria (**page 9**) established for genetic testing will be screened. The primary focus of this Facility will be to make available the resources and technical support to effectively evaluate high-risk families for inherited susceptibility to cancer. The function of the Facility will be to initially evaluate research participants for germ-line mutations in *BRCA1*. This confidential information will then be relayed to the appropriate investigators (as indicated in the previous sections) to aid in the clinical management of these mutant allele carriers. If a mutation is detected, the Facility will request that a second sample of blood will be donated to verify the initial finding. Once a mutation has been re-verified, genetic testing will be offered to other members of the research participant's family. Screening of other candidate susceptibility genes will proceed if initial testing warrants (e.g.,

negative for a *BRCA1* mutation, ample number of affected individuals collected to perform linkage to the *BRCA2*, *BRCA3*, and *OVCA1* loci, co-segregation of melanoma with breast and/or ovarian cancer, and co-segregation of breast and ovarian cancer with tumors commonly associated with the Li-Fraumeni syndrome, evidence of symptoms associated with ataxia telangiectasia. The specific methods for case identification and analysis are detailed below.

Family Selection Criteria: Based on our previous experiences, most of the current criteria used to select kindreds for evaluation may be much too restrictive. Therefore, we will evaluate: i) affected individuals with a family history of at least one first degree relative with either breast or ovarian cancer (any ages) or one second degree relative (maternal or paternal) with breast and/or ovarian cancer, ii) individuals affected with both breast and ovarian cancer, iii) unaffected individuals linked to *BRCA1*, and iv) unaffected individuals with a very strong family history of cancer (when affected individuals are not available).

Linkage Analysis: In order to establish probabilities of linkage, lod scores of linkage of predisposition to breast cancer and/or ovarian cancer to D17S855 will be computed using a previously described model (33). The distance between D17S855 (an intragenic polymorphism) and *BRCA1* is assumed to be 0cM (22). The probabilities of linkage used in the calculation will be 45%, 81% and 92% for families with 0, 1, and 2 cases of ovarian cancer, respectively (19,34). Lod scores for linkage to *BRCA2* will be computed as in (24).

DNA and RNA isolation: Genomic DNA will be prepared from 10mls of anticoagulant/acid citrate/dextrose treated blood samples as previously described (25). For the isolation of total RNA, ~20mls of peripheral blood lymphocytes will be purified using Histopaque 1077 (Sigma) followed by rinsing in cold serum free RPMI media. Half of the resulting cell pellets will be subjected to extraction with RNazol B as described by the manufacturer (Cinna, Biotecx Laboratories Inc.). The remaining half of the lymphocyte pellet will be resuspended in 90%FCS/10%DMSO and cryopreserved at -120°C. RNA will then be used for RT-PCR and PTT (if warranted) assays and DNA for SSCP and ASO analyses as described below.

Single-Strand Conformational Polymorphism (SSCP) Analysis: Initial studies will focus on identifying sequence alterations in *BRCA1* gene, however, depending on the types of cancers observed and the age of onset, other predisposing genes such as *ATM*, *TP53*, *CDKN2/MLM*, and/or *OVCA1* may be evaluated. In all cases, SSCP will be carried out as we have previously described (35, 36).

DNA Sequencing of Variant SSCP Bands: Variant SSCP bands will be excised, eluted, amplified by PCR and the product separated from primers using Wizard resin (Promega) according to manufacturer's specifications. The purified DNA will be sequenced using an automated fluorescence-based cycle sequencer (Model 377A Automated Sequencer, Applied Biosystems) and taq dye terminator chemistry. Sequencing primers will be the same as those used to amplify the template.

Direct DNA Sequencing of Genomic DNA: Constitutional DNA from a representative member of each family will be amplified using the appropriate PCR primers. In all possible cases, the individual selected for analysis will be affected with either breast and/or ovarian cancer. In cases where linkage to *BRCA1* has been established, genomic sequencing will be performed on DNA from an unaffected individual who has been shown to carry the *BRCA1* haplotype of risk. PCR and sequencing will be performed using the conditions described above.

Detection of Mutations by Incision of DNA Heteroduplexes with ARGDI: A) *Preparation of Mono Q Fraction of Celery Extracts.* One hundred grams of celery stalk is homogenized in a

Waring blender with 100mls of 0.1M Tris-HCl, pH 7.0 at 4°C for 2 min. The mixture is cleared by centrifugation and the supernatant is fractionated by anion exchange chromatography on a FPLC Mono Q column; the bound protein is eluted with a linear gradient of salt. The Mono Q fractions are tested for endonuclease activity (e.g., specific 3' cutting of all types of mismatches and 2, 3, 4, 5, and 8 base loops) and stored at -70°C. The Mono Q fraction of AGRD I is of sufficient enzymatic purity for the proposed mutation detection assay. However, further purification of the enzyme is in progress, and the enzyme is close to homogeneity after five purification steps. B) *Preparation of fluorescently labeled substrate. BRCA1* Oligonucleotide primer sets (37, 38) will be synthesized on Applied Biosystems Model 394 DNA Synthesizer; the forward primers will be labeled with FAM (6-carboxyfluorescein) amidite, a blue fluorescent dye and the reverse primers with TET (4,7,2',7'-tetrachloro-6-carboxyfluorescein) amidite, a green fluorescent dye. PCR will be carried out as described above except that fluorescently labeled primers will be used. C) *Mismatch Repair Endonuclease Assay.* Fifty nanograms of PCR product in 20µl of 25mM KCl, 10mM MgCl₂, 20mM Tris pH 7.4 is denatured at 95°C for 1 min and slowly cooled to room temperature to form heteroduplexes. 0.5µl of Mono Q fraction is added and incubated at 37 or 45°C for 30 min. One microliter of 200mM EDTA is added to terminate the reaction. The reaction is passed through a Centri-Sep column (Princeton Separations, Inc.) and dried under a vacuum. The pellet is resuspended in 0.5µl of Genescan 350 TARMA (N,N,N,N-tetramethyl-6-carboxyrhodamine) standard (ABI), 4µl of deionized formamide, and 1.2µl of blue dextran loading buffer. The sample is heated to 95°C for 3 min, quenched in ice water, and electrophoresed through a standard 0.4mm-thick, 24cm, 6% polyacrylamide gel run on a 373A DNA Sequencer (ABI) at 2500V, 30W, 40mA for 16 hours. Genescan 672 software is used to analyze the lanes and produce electrophoretograms. The internal standard DNA molecular weight markers allow size determination for each lane independently.

Allele-Specific Oligonucleotide Hybridization Analysis for Recurrent Germ-line Mutations: Potential mutations will be verified by ASO hybridization for the proband and all other participating members from their families, according to methods described elsewhere (22, 39, 40).

Haplotype Analysis: Haplotypes will be constructed by *BRCA1* mutant allele carriers for the chromosome 17q region containing the four microsatellites D17S855 (41) D17S1322, D17S1323, and D17S1327 (42, 43) by inspection of segregation patterns, and by assuming that a minimum number of crossovers will have occurred between these polymorphisms. STRPs will be typed by methods we have previously described (25, 44).

B. Establishment of a Data Management System

The data management system developed for the Registry is based on that which supports the FCCC Family Risk Assessment Program. The software employed maintains data on clinical information, health history, family data, socio-demographic and exposure information, and cancer screening practices. This system is capable of generating multigenerational pedigrees. The data which feeds pedigree generation is easily updated by include deaths or new cancers reported for previously listed family members, as well as new births. The software is also capable of creating the union of family histories provided by two or more distinct study subjects in the same family, in order to create an "extended" pedigree. The system uses the relational data base product Oracle as the primary software platform for data entry and validation, storage, retrieval, modification, and security. This software system runs on a UNIX-based distributed computing system consisting of multiple DecStation 5000 RISC processors managed and operated by the Research Computer Services group at FCCC. These multi-user systems are fully integrated into the FCCC computer network. This network supports a variety of software products including ORACLE, SAS, BMDP and IMSL and provides access to the global Internet. The data base for this Registry consists of a series of

14 tables linked by a common unique identifier. These tables include: (1) Health History Data, (2) Family History Data, (3) Clinical Data (i.e. tumor stage, grade, histology, ER, PR, treatment type, etc.), (4) Epidemiologic Data (i.e. smoking history, weight history, radiation exposure), (5) Reproductive History (i.e. age at first live birth, parity, etc.), (6) Socio-Demographic Data (i.e. age, sex, race etc.), (7) Diet Data, (8) Follow-up Data (i.e. survival, disease free survival, etc.), (9) DNA Data (i.e. date of DNA extraction, volume of blood extracted, DNA yield OD_{260}/OD_{260} , protein concentration, DNA concentration, μg DNA per vial, number of vials made, freezer location of vials, and buffer used to dissolve the DNA), (11) Frozen Specimen data (i.e. date of procurement, the wet weight of the tissue, the number of vials frozen, and freezer location), (12) Archived Tissue Data, (13) Plasma Data and (14) Shipping History Data. Several steps have been taken to assure quality of the data. A protocol has been established whereby the Registry data manager will supervise the data entry at FCCC. Validation of data takes place both during and after data entry. During data entry, validation occurs in four ways. Variable types such as numeric, character, or date are specified, and entry of a variable into a field is restricted to a specific type (e.g., character data may not be entered into a numeric field). For numeric and data variables, ranges are set; any value outside the range is rejected, and the error must be corrected before continuing with data entry. When character, numeric, or date data is entered, the value is checked against a list of all possible values. Data consistency will be further ensured when possible by making certain that mutually dependent fields contain logically appropriate data (e.g. death date must occur after birth date).

In order to preserve the privacy of the human subjects, a series of security procedures are undertaken. Only numeric identifiers are stored with study results. Lists of names and addresses are retained by the investigators in a secure location. Similarly, completed hard copy data collection instruments are stored in locked filing cabinets. ORACLE allows for a multi-level system of privileges whereby restrictions for each user can be implemented commensurate with their needs to access data. As studies expand, these privileges are reviewed by the Core professional staff. The Core staff take the issue of confidentiality very seriously and instruct all new personnel with any access to data, including laboratory technicians, in the ethics of electronic data access.

C. Development and Implementation of a Recruitment Strategy

Here we describe the developmental process including input from the Risk Advisory Panel, focus groups, survey data, and summaries of meetings with Medical Directors of Network institutions. The findings presented below have provided essential information to assist in the development and implementation of a Recruitment Strategy for the High Risk Registry.

1. Formation of a Risk Advisory Panel

In order to have input from the inception of the project, a Steering Committee for the Risk Advisory Panel was established in September of 1994. The purpose of the Steering committee was two-fold: (1) to provide preliminary guidelines for the implementation process; and (2) to initiate the establishment of the Risk Advisory Panel.

The implementation process was discussed during the September and October meetings of the Advisory Group Steering Committee (**See Appendix B for a listing of members**). As a result of these discussions, it was decided that the main implementation tasks for the first year of the project were to: conduct a focus group and survey with Network Managers to assess programmatic and administrative issues as well as current procedures and practices utilized for cancer control by the Network hospitals that could serve as a foundation for implementation; establish basic criteria for participation in order to offer the Network

hospitals a framework for expected tasks, staffing, and service needs; target 4 to 5 Network institutions who expressed interest in the High Risk Registry to determine desired level of participation, and to pilot the individualized implementation process.

The Steering Committee additionally submitted names of potential participants and established the purpose of the panel. The main goal was to establish a group of experts that could respond to the variety of issues and concerns that could arise with providing familial cancer risk assessment and establishing a risk registry. It was expected that the group would meet as a whole annually and that special issue groups would be convened on an ad hoc basis. The steering committee identified several areas for representation on the panel. These included consumers and experts in the areas of oncology, nursing, genetics, genetic counseling, psychology, the law, health insurance, policy development, and ethics. A list of names was compiled and at the end of Year One, potential participants were mailed letters and invited to serve on the panel. The Risk Advisory Committee will begin its formal work in Year Two.

2. Focus Group with Network Program Managers

A focus group was conducted on 10/28/94, with a total of 14 program managers attending a Quarterly Network Meeting at the Fox Chase Cancer Center. The purpose of the focus group was to describe the High Risk Registry project, to clarify issues related to the program components and to identify barriers and facilitators to program implementation. The program was received with real interest and the program managers presented helpful information on strategies that have been successful for integrating new programs into the Network hospitals. A summary of administrative issues, barriers and facilitators are presented in **Table II**. Findings from the focus group helped identify related issues for the procedures development that included: (1) training for staff, (2) addressing re-imbursement issues with administrators, (3) providing staff with a step-by-step process for implementation, and (4) making educational and implementation resources "user friendly" with materials such as script for education and standardized forms or letters.

3. Survey with Network Program Managers

An open-ended survey questionnaire was designed to identify programmatic and recruitment practices that could be adapted for the High Risk Registry Program. The questions were developed to obtain information in the following areas: (1) the types of prevention programs that Network hospitals currently provide, (2) current recruitment strategies for established prevention programs, (3) risk assessment tools utilized in community hospitals, (4) family history documentation and record keeping practices, (5) current follow-up for individuals at risk for cancer, (6) availability of genetic counseling services, and (7) appropriate providers and other key staff to involve in the High Risk Registry Program. The questionnaire was given to the 14 program managers at the 10/28/95, Quarterly Network Meeting with a 100% response rate. Since the questionnaire was open-ended, all responses were listed and common answers were categorized. The responses were then listed in order of greatest numerical frequency. A summary of the selected survey findings are found in **Table III**. These findings revealed that we could build on previous cancer control programs, marketing, and recruitment strategies. A risk assessment tool and documentation process needed to be established. Primary care providers needed to be involved in the process to make the program viable. Standardized screening recommendations were necessary along with staff training in the Familial Cancer Risk Assessment. Oncology Nurses were identified as key to program implementation.

Table II Focus Group Findings: Issues Related to Program Implementation

| | |
|-----------------------|---|
| Administrative Issues | |
| | Cost to the Network hospital to implement the Risk Registry |
| | Legal Liability related to risk counseling |
| | Resources needed, i.e. staffing, support services, supplies, training, educational tools |
| Barriers | |
| | Lack of re-imbursement for enrolling women into the Risk Registry |
| | Ability to get a program like this approved through Internal Review Board |
| | Medical recommendations once someone is identified as high risk |
| | Ability to obtain re-imbursement for medical follow-up and screening for high-risk population |
| Facilitators | |
| | Involving primary care providers and gynecologists as part of the implementation since they will be referrers and gatekeepers |
| | Naming a primary care provider as coordinator or medical director provides buy-into program |
| | Assist the Medical Director of the Cancer Center to determine level of participation with his/her own administration and staff. |
| | Provide standardized forms, e.g. consent forms, protocols, patient letters |
| | Educational tools, such as slides and script |

Table III Selected Survey Findings: Implementation and Recruitment Issues * (N=14)

| <u>Area Questioned</u> | <u>Response</u> | <u>Total</u> |
|--|--|--------------|
| Current prevention programs | BCPT | 11 |
| | PCPT | 11 |
| | Cancer Screenings | 5 |
| Recruitment Medium | Newspaper | 9 |
| | Education sessions | 8 |
| | Physician referral | 6 |
| Current Cancer Risk Assessment tool | None | 5 |
| | Routine H&P | 5 |
| | ACS brochure on cancer risk | 1 |
| Documentation of Cancer Family History | Not done | 5 |
| | H & P form | 5 |
| | Tumor Registry | 2 |
| Current recommendations for high-risk individual | Refer to Fox Chase | 8 |
| | None | 2 |
| | Follow recommendation of their Physician | 2 |
| Current genetic counseling service | In perinatal services | 4 |
| | No service | 4 |
| | Don't know | 4 |
| Appropriate provides to involve | Family Practice | 12 |
| | Oncologists | 11 |
| | Gynecologist | 9 |
| Key hospital staff to involve | Nursing | 10 |
| | Administrators | 7 |
| | Medical | 4 |

* Findings presented here represent the three highest responses.

4. Criteria for Level of Participation

With the assistance of the Advisory Steering Committee three levels of participation were established to allow the Network Hospitals to initiate the High Risk Registry Program in a way that could be tailored to their individualized resources and cancer control services. These included:

Basic level - identification of high risk individuals with referral to FCCC for risk assessment services and entry into high risk registry

Intermediate level - identification of high risk individuals, provide education about risk, and conduct familial cancer risk assessment, identification of families appropriate for genetic studies and referral to FCCC for blood collection, testing and results (if warranted).

Advanced level - identification of high risk individuals, provide education about risk, and conduct familial cancer risk assessment, identification of families appropriate for genetic studies and send blood/tissue samples for genetic testing, and establish follow-up cancer risk services in which context pre/post counseling could be provided.

5. Meeting with Medical Directors

An overview of the DOD High Risk Registry grant was presented to the Network Affiliate Medical Directors in their October 1994 meeting and the criteria for the level of participation were reviewed. Comments from this meeting suggested that an individualized approach was a appropriate format for initiating an implementation process. Four Medical Directors expressed interest in the program following this meeting and were targeted for implementation for the first year. These included:

Delaware Country Regional Cancer Center, Drexel Hill, Pennsylvania
Hunterdon Regional Cancer Center, Flemington, New Jersey
Montgomery Cancer Center, Norristown, Pennsylvania
Paoli Cancer Center, Paoli, Pennsylvania

During January 1995 through March 1995, meetings were held at these Network institutions. Each of the meetings were attended by the Medical Director along with administrative and nursing staff to discuss implementation. All four cites indicated an interest to participate initially at the intermediate level with hopes to move to the advanced level. They also expressed interest in committing staff and resources to establish the High Risk Registry Program. The preliminary process for implementation at the four hospitals was to pilot the High Risk program on a small scale with referrals from the cancer centers. The Medical Directors preferred to test out the process before they developed a marketing plan. A Genetic Counseling Protocol and an IRB approved informed consent (**Appendix C**) was provided so that the Medical Directors could obtain IRB approval from their respective institutions.

These meetings with the Medical Directors enabled us to identify five tasks necessary to pilot the implementation process. These tasks included:

1. Develop a Risk Assessment tool
2. Conduct a training for Network nurses in Familial Cancer Risk Counseling
3. Develop and disseminate scripted educational materials for educating women about risk for breast cancer
4. Provide standardized format for recruitment into the High Risk program
5. Provide a protocol for genetic risk assessment and testing.

The following sections describe the development process designed to achievement the above tasks. It is important to note that following the Nurses Training (**described on page 15**), six additional Network hospitals (listed below) expressed interest in the program. Subsequent meetings were held in September 1995 with Medical Directors and staff from the Community Medical and Polyclinic Regional Cancer Centers. Meetings with the four remaining hospitals have been scheduled for the October and November of 1995.

Community Medical Regional Cancer Center, Toms River, New Jersey
Memorial Regional Cancer Center, Moorestown, New Jersey
PolyClinic Regional Cancer Center, Harrisburg, Pennsylvania
The Reading Hospital Regional Cancer Center, Reading, Pennsylvania
Riverview Regional Cancer Center, Redbank, New Jersey
St. Luke's Regional Cancer Center, Bethlehem, Pennsylvania

6. Risk Assessment Tool

The Steering Committee of the High Risk Advisory Panel helped to establish essential components to include in a risk assessment tool for the high risk registry. The areas included: family, exposure, medical, and reproductive histories; screening practices; and perception about risks for cancer. We embarked on a process to identify a self-administered risk assessment tool that would include the majority of these areas. This process included exploring the options of using an existing cancer risk assessment form, adapting the risk assessment tool used in Family Risk Assessment Program (FRAP) as well as exploring the potential for making the existing FRAP form into a scannable document.

No existing tool was found to meet the above criteria. The option to computerize the existing FRAP risk assessment tool would have been an expensive proposition and the scannable format posed numerable problems for administration across diverse populations, and for quality assurance in data entry. Therefore, the existing FRAP risk Assessment tool was revised for use in the High Risk Registry program.

The questionnaire includes a brief description of the High Risk Registry program with informed consent to collect personal and family medical history. It is formatted for ease of completion with explanations and instructions preceding each section. Peer review of the questionnaire was conducted by medical oncologists, nursing staff, genetic counselors and health educators. It was then pretested with 10 women having a family history of breast cancer. Final revisions were made in July 1995 (**See Appendix D**), and the tool was disseminated to the four Network hospitals targeted to pilot the implementation process .

7. Nurses Training

An essential part of implementing the High Risk program at the basic level was to have nurses from the Network hospitals trained to identify high risk individuals. The training for Nurses in Familial Cancer Risk Counseling was conducted in two phases: 1) development and implementation, and 2) evaluation.

During the development phase three focus groups were conducted with a total of 18 Network nurses from in-patient and outpatient oncology service, gynecology practice, primary care and health promotion settings. The objectives of the focus groups were (1) to identify the current role of nurses in cancer risk counseling, (2) to obtain feedback regarding areas for the course content, and (3) to identify issues for clinical application. Findings from the focus groups indicated that nurses had received little or no formal training in cancer genetics. Nurses routinely obtained information about cancer family history. However, there was no systematic

way to document nor utilize the family history information as part of the patient's plan of care. Feedback on the course content indicated that nurses needed a refresher on principles of genetics, and indicated that skills for taking a comprehensive cancer family history, developing family pedigrees and communicating risk were essential. Additional issues identified were medical management of high risk individuals, the psychological impact of cancer risk information, the legal and ethical implications, and administrative issues in establishing cancer risk registry services.

Based on this information a curriculum for a Training program in Familial Cancer Risk Counseling was developed to provide the Network nursing staff with the knowledge and skills needed to provide Familial Cancer risk Assessment and Counseling. The course was designed to assist the nurses to identify and assess the risk for familial cancer, to learn the skills of obtaining a comprehensive cancer family history and developing cancer pedigrees, to communicate cancer risk to high risk individuals, and to understand medical management issues in high risk populations. **(See Appendix E, for Training Manual)**

The three-day training program was conducted with a total of 36 oncology nurses, including 10 nurses from eight Network hospitals. Of these, only one nurse had ever taken a formal course in genetics. To evaluate the training program, a pre/posttest measure of knowledge and subjective evaluation of the course objectives were used. There was a statistically significant improvement in pre and posttest knowledge scores ($P = .0001$) using the Wilcoxon signed rank statistic, with a mean pretest score of 54% and a mean posttest of 75%. The course objectives were rated "completely met" by 85% of the nurses. There was great enthusiasm expressed by the nurses attending the course to incorporate the training into services offered by their hospitals. The interest by the nursing staff proved to be an important piece in garnering support for the high risk registry program. Following the training, six Network institutions contacted Fox Chase and expressed interest in implementing the High Risk Registry Program. Those nurses who received the training have subsequently been named as staff coordinator at their respective Network institution. Furthermore, an abstract describing the development and outcomes of the nurses training was submitted to the Oncology Nursing Society **(See Appendix F)**.

8. Scripted Education Materials

Although the development and dissemination of the educational materials were slated as a task for the second year of the project, the education sessions became an essential vehicle for recruiting women into the HRR program. Therefore, this task became a priority to complete in the first year. The following describes the development and dissemination of the educational tools.

The breast cancer risk education flip chart was designed as a vehicle to recruit women into the High Risk Registry Program. The Network staff viewed the education session as a critical piece both to explain the risks for breast cancer and for the purpose of the High Risk Registry program. Additionally, the focus group with the Program Managers had noted that this format was similar to the recruitment process for the Breast Cancer Prevention Trial (BCPT) where education about breast cancer risk and introduction to the BCPT facilitated recruitment. Therefore, it was necessary to provide the education materials to pilot a recruitment process. Prior to developing the flip chart, a series of focus groups was conducted with women who had a family history of breast cancer. The participants identified topics of concern and questions to be answered. They also provided feedback about the presentation format for the information. Based on this input, a flip chart of text and graphics was created to cover: 1) normal anatomy and development of the breast, 2) breast cancer risk factors, 3) the genetic origins of cancer, 4) early detection and 5) prevention. **(See Appendix G)**

The section on the normal anatomy and development of the breast discusses the breasts' glands and ducts and the hormonal influences related to menstruation, pregnancy and menopause. Benign breast conditions are also discussed. This is followed by a discussion of the factors known to affect breast cancer risk, as well as those still under study. A thorough discussion of positive family history of breast cancer leads into a description of the genetic origins of breast cancer. A brief overview of DNA, chromosomes and genes is provided. Pedigrees showing sporadic, familial, and hereditary cancer patterns are reviewed, and the importance of locating genes related to cancer is explained. An overview of genetic testing for cancer includes a review of its benefits and limitations.

The next section emphasizes the importance of early detection and reviews cancer screening recommendations with particular attention to screening high risk woman. The benefits of mammograms, clinical and breast self examination are covered. The final section discusses prevention options including lifestyle changes, the Breast Cancer Prevention Trial and prophylactic surgery and the option for further risk assessment as part of the Risk Registry Program. Women are instructed that dietary fat and breast cancer risk is still under study, as is the use of Tamoxifen as a chemopreventive agent in women who have never had breast cancer. The discussion of prophylactic mastectomy emphasizes the lack of information about the efficacy of the procedure and raises some of the issues women should consider when exploring this option.

The educational materials, script, table of contents and sample pedigrees were made available to the four Network hospitals targeted for year one implementation. Each hospital received a set of the materials on Macintosh discs formatted for both color slides or 8.5x11 color prints. This gave the Network facility two presentation formats to use, an easel binder, flip chart or slides. The educational flip chart continues to be modified to accommodate new information about genetic mutations related to breast cancer, and other risk factors. The discovery of the BRCA1 gene prompted changes to expand the genetic component and provide more information about the potential for genetic testing.

9. Procedures for Recruitment into High Risk Registry Program

The Network hospitals targeted for implementation during the first year had indicated an interest to participate at the Intermediate level. Components for this level of participation included: (1) identification of high risk individuals, (2) provision of education to high risk individuals about familial cancer risk, (3) conducting familial cancer risk assessment, with the identification of families appropriate for genetic studies, and (4) referring participants or sending blood or tissue samples to Fox Chase Cancer Center for testing and results (if warranted). An outline of the components for Implementation and Recruitment are outlined below with the procedural tools noted in italics (**Procedures for Implementation, See Appendix H**).

1. Identify individuals with a family history of breast cancer via media or physician referral.
Draft brochure, "What your family history can tell you about Cancer", designed to be adapted by the Network Facilities.
2. Initial phone contact -
Baseline phone script
3. Schedule individuals for educational session and mail confirmation letter along with risk assessment tool to be completed prior to education session
 - a. *Standardized confirmation letter with description of program*
 - b. *Health History Questionnaire (Appendix D)*

4. Conduct group education session.
 - a. *Instructions for reviewing Health History Questionnaire*
 - b. *Instructions for conducting group education session*
5. Send Completed Family Risk Assessment tools to Fox Chase
 - a. *Instructions for following group education session*

To date, the education materials, standardized forms for recruitment, protocols for genetic risk assessment and informed consent have been disseminated to the four network hospitals targeted for implementation in the first year. The Delaware County Regional Cancer Center conducted their first education session on July 25, 1995. The Montgomery and Paoli Regional Cancer Centers have scheduled their first education session to pilot the implementation and recruitment strategies for the Fall of 1995. Actual recruitment is now underway and will proceed into Year Two.

Conclusions

The work of Year One of the High Risk Registry Program has laid the groundwork for implementation. The establishment of the registry has launched the effort to test educational and counseling strategies that can best meet the need for information that will accompany the identification of breast cancer susceptibility genes.

The Breast Cancer Risk Registry Testing Facility has established protocols for collection, transportation and processing of blood samples. In addition, the data management system is in place to receive health history, family history and clinical data. These protocols have not yet been tested within the Registry Program. Since recruitment was initiated at the end of Year One, we will be testing and adapting these protocols as needed in Year Two.

The development process for implementation strategies has revealed both interest and enthusiasm on the part of the Network hospitals to be part of this research to expand our epidemiologic and biologic knowledge about modifiable causes of breast cancer. We have learned that we can build on previous work in cancer control within community settings, such as the BCPT and PCPT programs. Based on this experience, the community hospital staff had the expectation that all materials, form letters, forms for patient contacts, protocols and educational tools would be available for them. For this reason, it was necessary to develop and disseminate the educational materials in Year One rather than Year Two. As part of the dissemination of the educational materials with its genetic risk component, we also learned that a mentoring system needed to be established between the Network Nurse Coordinator and the High Risk Registry project manager. This mentoring included a practice session or demonstration of the educational materials, attendance at the first education session scheduled by the Network hospital to provide observation and feedback on their presentation and assistance with the implementation procedures for reviewing the Health History Questionnaire and processing these forms. The project manager will take on the added responsibility in Year Two to provide this mentoring process as each new Network institution implements the High Risk Registry Program.

Now that the recruitment of women into the High Risk Registry Program is underway, efforts will now be focused on developing, implementing and evaluating the breast cancer risk counseling interventions. These interventions will include protocols for preparing individuals for genetic results and providing genetic feedback to individuals and families. This next step will serve as a catalyst for transferring information generated by the Human Genome Project into the realm of community practice.

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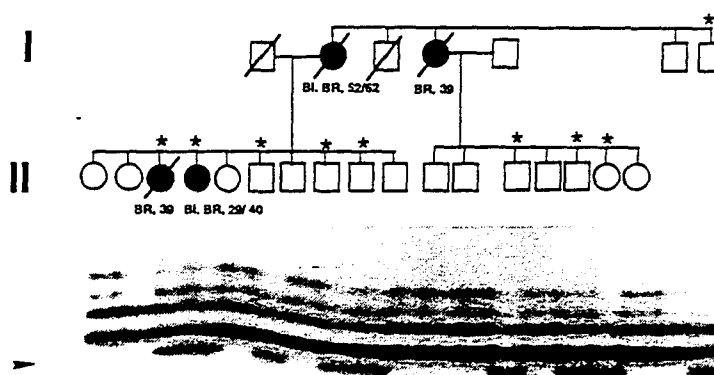
Appendices

- A. Figure 1.
Figure 2.
- B. Advisory Group Steering Committee
- C. Genetic Counseling Protocol with Approved IRB Informed Consent
- D. Health History Questionnaire - Family Risk Assessment Tool
- E. Training Manual for Familial Cancer Risk Training Program for Nurses
- F. Abstract Submission Regarding Nurses Training in Familial Cancer Risk Counseling
- G. Breast Cancer Risk Education Materials and Script
- H. Procedures for Implementation and Recruitment
 - a. Brochure - "What your family history can tell you about cancer"
 - b. Baseline Phone Script
 - c. Confirmation letter for group education session
 - d. Instructions for the Health History Questionnaire
 - e. Instructions for conducting the group education session

APPENDIX A

Figure 2. Segregation of a *BRCA1* exon 11 SSCP variant in kindred 389 (partial). Only living individual's samples were evaluated. The frameshift mutation, 4184del4, indicated by the lower additional band was present in all of the women affected with early-onset breast cancer (the carrier status of the deceased individuals are inferred), one of the asymptomatic women, and six asymptomatic males. Solid circles represent women with cancers; open circles cancer free individuals; open boxes disease free males; diagonal lines through circles or squares represent deceased individuals; ages shown for each woman are at age of diagnosis. Br, breast. Asterisks indicate carriers of the mutant *BRCA1* allele.

FAMILY 389



FAMILY 83

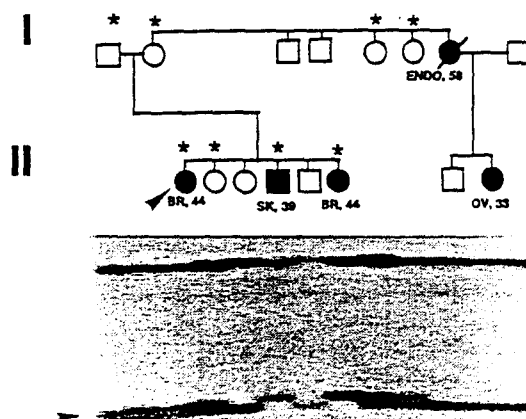


Figure 3. Segregation analysis of an exon 11 SSCP variant in kindred 83 (partial). The missense mutation, R1347G, was present in both women with bilateral breast cancer, a male with skin cancer, and four asymptomatic females, but was absent in the proband's aunt with endometrial cancer and her daughter affected with early-onset ovarian cancer. Two of the seven mutant allele carriers were homozygous for the missense mutation (lanes 6 and 8). The proband's father also has a family history of cancer which is not shown; a mother with ovarian cancer, a father with lung cancer, and a nephew skin cancer. Symbols are as described in Figure legend D. Arrow in generation II indicates the proband. Cancers are indicated as follows: Br, breast; Ov, ovarian; Sk, skin; End, endometrial.

APPENDIX B

High Risk Registry Advisory Panel Steering Committee

| | |
|------------------|-----------------------------------|
| Mary Daly | Fox Chase Cancer Center |
| Mary Connelly | Fox Chase Cancer Center |
| Sandra Gandsman | Fox Chase Cancer Center |
| John Sprandio | Delaware County Memorial Hospital |
| Andrew Godwin | Fox Chase Cancer Center |
| Eric Ross | Fox Chase Cancer Center |
| Margaret O'Grady | Fox Chase Cancer Center |
| Suzanne Smith | Delaware County Memorial Hospital |

Genetic Cancer Risk Counseling Protocol (FCCC) for Hereditary Breast and Ovarian Cancer

A. Entry into Program

Entry into the Family Risk Assessment Program (FRAP) includes collecting sociodemographic, risk perception, and risk comprehension data, a personal medical history and a family history of cancer. Existing cancer screening practices are determined, and the consultand's general psychological adjustments, risk-specific psychological distress patterns, and existing coping styles are measured through a set of questionnaires.

It is at this point that a FRAP chart for the consultand is established

Purpose: As a first step for cancer risk assessment, sociodemographic, risk perception, and risk comprehension data, personal medical history and family history of cancer are collected. Existing cancer screening practices are determined, and consultand's general psychological adjustment, risk-specific psychological distress patterns, and existing coping styles are measured through a set of questionnaires.

1. Initial Contact (1 hour; via telephone)
 - a. FRAP Participant Contact Log
2. Baseline Assessment
 - a. Health History Questionnaire (HHQ)
 - b. Psychology surveys
 - c. Diet survey
 - d. FRAP chart for consultand established

B. Education Session (approximately 2 hours)

At the initial educational session, basic information about the Family Risk Assessment Program is given. The education session provides information on the biological and environmental risk factors associated with breast and/or ovarian cancer. As well, the genetic factors associated with carcinogenesis, the influence of family history on one's risk for cancer, and the options available for prevention and early detection, are explained. An individualized carefully computed estimate of personal risk for breast cancer (the "Gail Model" score) is presented to the consultand attending the group education session for breast cancer. Each participant is invited to pursue further individualized assessment and counseling through the Family Risk Assessment clinic.

Purpose: Basic information about the Family Risk Assessment Program are given. The education session includes information on the biological and environmental risk factors associated with breast and/or ovarian cancer are provided in this session. As well, the genetic factors associated with carcinogenesis, the influence of family history on one's risk for cancer, and the options available for prevention and early detection, are explained. An individualized carefully computed estimate of personal risk for breast cancer (the "Gail Model" score) is presented to the consultand attending the group education session for breast cancer.

1. Education Session
 - a. Biological
 - b. Environmental
 - c. Genetic
 - d. Gail model score (presented during education session for breast cancer)
 - e. Descriptions of options recommended for early detection and prevention

C. Triage: Preliminary Clinical Risk Diagnosis (performed 1 day prior to Individual Counseling Session)

Purpose: Prior to the consultand's individual counseling session, the team members of FRAP formulate a preliminary clinical risk diagnosis based on an initial viewing of the family history. A cancer genetic family pattern/category of sporadic, familial, or hereditary is determined so that a plan for the appropriate type of cancer risk counseling strategy and testing research, best suited for the consultand, can be planned.

1. Triaging families

D. Individual Counseling Session (approximately 1 hour)

Purpose: During this session, detailed medical and family histories are obtained. Counseling is provided to explain risk for cancer based on findings from the medical and family histories. The current research to identify genes for breast and ovarian cancer, and how eligible individuals and their families can participate, are explained. Collection of blood and/or tumor samples from the consultand and from eligible family members is undertaken.

During the consultand's individual counseling session, the counselor obtains detailed medical and family histories. Using a computer generated pedigree as a working template, the family history is expanded. Confirmation of names, degree of relationship, and ages of relatives, and obtaining information on their medical, reproductive, and surgical histories are obtained. The consultand's personal medical history, including her reproductive history, medication and hormone usage, present occupation, lifestyle habits (smoking, alcohol, and drug usage) and about her general health, is documented.

Counseling is provided to explain risk for cancer based on findings from the medical and family histories. The genetics counselor explains the possible pattern or patterns of inheritance of cancers pertaining to the consultand's family history. Autosomal dominant inheritance, chromosomes, genes, and the concept of multifactorial reason for familial cancers (ie., multiple cancer susceptibility genes influenced by environmental agents) are described. The risks, benefits, limitations, and present status of genetic testing for cancer predisposition are explained. Issues of insurability and employability, cost of the test, and anticipated concerns within family members are explored.

Linkage analysis research to identify genes for breast and ovarian cancer in families, and how eligible individuals and their families can participate, are explained. If such research is feasible for the family, steps used in the collection of blood and/or tumor samples from the consultand and from family members eligible for linkage analysis, is undertaken, including an explanation on how these samples will be obtained and describing the medical consent forms.

It is at this point that a FRAP genetics chart for the consultand is established

1. Introduction - purpose of individual counseling session is explained
2. Personal medical history is obtained
 - a. general health (birth defects, heart, thyroid, history of surgeries, biopsies)
 - b. reproductive history
 - c. medication, hormone usage
 - d. smoking, alcohol, drug usage
3. Family history is obtained
 - a. a computer generated pedigree is used as working template
 - b. confirmation of names and ages of relatives
 - c. ethnicity and/or ancestral origins
 - d. consanguinity
 - e. confirmation of full sibship, relations
 - f. medical, reproductive, and surgical histories of family members
 - g. document environmental exposures (smoking, alcohol, work, war, etc.)
 - h. form(s) are signed to obtain medical records, when indicated
 - i. form(s) are signed to obtain tumor or biopsy tissue, when indicated
 - j. include recent changes to original HHQ and FRAP database
4. Cancer Genetics Counseling
 - a. explain pattern of inheritance of cancers in consultand's family history
 - b. autosomal dominant inheritance (how it pertains to family history)
 - c. explain chromosomes, genetics, linkage analysis
 - d. explain steps in linkage analysis process/protocol (letter announcing availability of results, pre- disclosure and disclosure sessions, follow-up)
 - e. inform of risks, benefits, and limitations of results from genetic testing
 - f. discuss concerns (confidentiality, insurance, psychosocial, impact of results)
 - g. answer questions, discuss issues raised (feasibility, family dynamics, etc.)
 - h. obtain informed consent and first blood sample from consultand
5. Contact family members for blood and/or tumor samples
 - a. Relative Identification Form (RIF)
 - b. Steps used to contact family member are explained:
 - i. letter accompanying blood collection kit and instructions
 - ii. instructions for collecting and mailing blood samples
 - iii. lab request for blood samples
 - iv. medical consent form
 - v. form to sign for release of medical records (if affected)
 - vi. form to sign for release of tumor sample (if affected)

E. Pedigree Review Committee Meeting

A summary of the consultand's individual counseling session and information from her medical and family histories is presented. A clinical risk diagnosis based on this information is reviewed, evaluated, and finalized with this committee, which consists of a multi-disciplinary team of medical oncologists, oncology nurses, health educators, cancer genetics counselor and

molecular geneticists. This team also helps to formulate follow-up recommendations for genetic investigation and counseling of all families seen by cancer genetics counselor.

Cases are reviewed periodically as new information is added to the data base.

Purpose: The consultand's medical and family histories and clinical risk diagnosis are reviewed, evaluated, and finalized with this committee, which consists of a multi-disciplinary team of medical oncologists, oncology nurses, health educators, cancer genetics counselor and molecular geneticists. This team also helps to formulate follow-up recommendations for genetic investigation and counseling of all families seen by cancer genetics counselor.

1. Pedigree Review Committee meeting.
 - a. information obtained from Individual Counseling Session is presented
 - b. confirming clinical risk diagnosis with Pedigree Review Committee
 - c. completing genetics consultation report
 - d. re-convene with Pedigree Review Committee as new information on consultand's medical and family histories are obtained

F. DNA Analysis and Disclosure of Test Results (6 to 12 months)

A letter is sent out to the consultand announcing the availability of results from the genetic testing and is advised to call the genetics counselor up to schedule an appointment for a pre-disclosure counseling session. During this session, issues previously discussed in the individual counseling session are summarized. During this session, the counseling team helps the consultand(s) to examine anticipated psychosocial and emotional concerns and impact from positive or negative test results for her and her family. If test results are still wanted, the counselor determines the type of disclosure preferred by the consultand (phone, letter, physician, etc.) and a date for the disclosure of test results is arranged. Support systems available to the consultand are identified during this session.

Before the results are disclosed in the disclosure counseling session, the consultand is asked if the results are still wanted. The test results are communicated in an appropriate manner with adequate time for answering questions and concerns. Options for medical and psychological follow-up are re-evaluated. The consultand(s) is/are reminded of availability of support and information resources and of the possibility that genetics counselor will recontact and address future genetic risks as they become known.

Purpose: The pre-disclosure session serves to help the consultand examine anticipated psychosocial and emotional concerns and impact from positive or negative test results for her and her family. Role play is included as a form of cognitive-affective processing to help the consultand get in touch with the reality of the impact of these results to her family and to other family members.

1. Announcement of availability of test results
 - a. letter or phone call announcing test results available to be disclosed
 - b. appointment date for the pre-disclosure counseling session is arranged

2. Pre-disclosure counseling session (approximately 1 to 1 1/2 hours)
 - a Summary of BRCA1 genetic test (what is a gene, gene alteration, etc.);
 - b the risks and benefits of receiving an increased risk or a decreased risk for inheriting or carrying a cancer susceptibility gene;
 - c the risks and benefits of not receiving any results from this study;
 - d limitations of test results, possibility of error;
 - e early detection options;
 - f life and health insurance coverage;
 - g the issues of confidentiality among family members, friends, employers;
 - h relaying information to primary physician
 - i examine existing support systems, psychology referrals presently available (make appropriate referrals when indicated)
 - j Role play examining:
 - i the psychological impact of carrier status information
 - ii the psychological impact of non-carrier status information
 - iii the psychological impact for reasons to not know the results;
 - iv possible impact on family dynamics;
 - k ask if test results are still wanted
 - l determine type of notification of result for proband
 - m disclosure date of test results to proband is set-up
3. Disclosure of test results counseling session (approximately 1 to 1 1/2 hours)
 - a introduction
 - b determine if results are still wanted
 - c the result is communicated in the presence of oncologist, counselors
 - d re-summarize implication of results
 - e re-summarize preventative and early detection options
 - f answer questions, concerns
 - g inform of availability of genetics counselor and their support resources (referrals) to address issues and concerns as they arise
 - h. inform possibility that genetics counselor will recontact and address future genetic risks as they become known
 - i inform consultand of upcoming follow-up questionnaires

G. Follow-up

Long-term follow-up is considered crucial for the medical and psychological well-being of individuals undergoing genetic testing. The purpose of the follow-up is to evaluate and report any changes in the consultand's previously measured general psychological adjustment, risk-specific psychological distress, and coping style. Up-to-date information/records on changes in medical and family histories since the disclosure of the test results are also obtained. Further information on adherence to recommended screening and preventive regimens, experiences with regard to issues of insurability, employability, and other potential forms of discrimination since the disclosure of genetic test results, is collected.

Contact is made by phone 1 week after disclosure of test results to clarify issues and identify acute problems and intervene when appropriate. Follow-up visits at 6 and 12 months are held to further assess medical, educational, and psychological needs. In addition, counseling

support is made available on an ad hoc basis to address concerns as they arise. Access to physicians, a social worker, and psychologist, in addition to the genetics counselor, is available.

Purpose: To evaluate and report any changes in consultand's previously measured general psychological adjustment, risk-specific psychological distress, and coping style. Up-to-date information/records on changes in medical and family histories since disclosure of test results are obtained. Further information on adherence to recommended screening and preventative regimens, experiences with regard to issues of insurability, employability, and other potential forms of discrimination since disclosure of genetic test results, are obtained.

1. Short-Term Follow-up (1 to 2 weeks post-disclosure)
 - a. Phone call or visit with cancer genetics counselor to discuss short term impact(s) of test results, change(s) in screening practices, follow-up with options, effectiveness and usage of psychological follow-up, etc.
 - b. Questionnaire filled out when applicable.
 - c. inform of availability of genetics counselor, medical, psychological, and support resources to address issues and concerns as they arise (referral for psychological assessment made here, when indicated)
2. Long-Term Follow-up (20 to 24 weeks post-disclosure)
 - a. Phone call or visit with cancer genetics counselor to discuss long term impact(s) of test results, change(s) in screening practices, follow-up with options, effectiveness and usage of psychological follow-up, etc.
 - b. Questionnaire filled out when applicable.
 - c. re-inform of availability of genetics counselor, medical, psychological, and support resources (referrals) to address issues and concerns as they arise.
3. One Year Follow-up (50 to 54 weeks post-disclosure)
 - a. Phone call or visit with cancer genetics counselor to discuss long term impact(s) of test results, change(s) in screening practices, follow-up with options, effectiveness and usage of psychological follow-up, etc.
 - b. Questionnaire filled out when applicable.
4. Support sources (social worker, genetics counselor) available to individual as needed

APPENDIX C

Informed Consent to Participate in Research Studies

- 1 **Title of Study:** Genetic Testing for Predisposition to Hereditary Forms of Cancer.
- 2 **Principal Investigators:** Mary B. Daly, MD, PhD
Andy Godwin, PhD
Josephine Wagner, BS, MS
Family Risk Assessment Program
Fox Chase Cancer Center
510 Township Line Road
Cheltenham PA 19012
tel: (215) 728-2705 or (800) 325-4145
- 3 **Description:** On _____, I donated a sample of my blood for a genetic research study titled: "Genetic Testing for Predisposition to Hereditary Forms of Cancer". I have been notified that genetic test results from that study are now available to me and that I now can choose to learn the results of these tests.
- 4 **Potential Limitations:** I understand that the results from these tests are not 100% accurate. A negative test result (meaning, no gene mutation associated with the likelihood of developing cancer is found) does not eliminate the chance that I might have a mutation in another gene which has not yet been discovered. Even if I do not have any gene mutation, I am still at some risk of developing cancer. Likewise, a positive test result (meaning, a gene mutation associated with the likelihood of developing cancer is found) does not mean that there is a guarantee that I will develop cancer. Although I will be given recommendations about early detection methods based on my test results, I realize that these suggestions are still preliminary, and may change as time goes on.
- 5 **Potential Benefits:** By examining my sample of blood for a genetic mutation, it may be possible to determine if I and/or other members of my family have inherited a form of a gene that is related to certain kinds of cancer. I have the option to participate in this second phase of this research study and receive genetic counseling along with the test results. The information and interpretation of these test results can help me and my family members (if they wish) to know if we are carriers of a gene mutation associated with cancer predisposition, what cancers we would be at risk for, and what are the options available to us for prophylactic surgery, screening, and early detection of these cancers. The information I receive may help to decrease my anxiety about my risk for developing cancer by giving me a more reliable estimate of my risk. The cancer genetics counselor is a qualified professional trained in the genetic assessment and counseling for cancer risk. This counselor will be available to address any issues, concerns or anxieties I or my family may have about the information. I understand that there is the possibility that the cancer genetics counselor will recontact me and go over future genetic risks as they become known.

6 Potential Risks: I understand that at present, there are no clear statements available regarding risks related to one's employability and insurability, based upon receiving results from genetics testing for cancer predisposition. If I test positive for a carrying a gene mutation associated with cancer predisposition, there may be the possibility that existing insurance rates may increase, existing policies may be at risk of being canceled, or there may be some difficulty in obtaining new health or life insurance policies when changing jobs. Insurance companies and/or employers may in the future decide to ask if I have ever had a genetic test for cancer susceptibility when I apply for a new policy or a new job. There is the possibility that tension may be created with other members of my family who learn about the results of these tests. There is also the risk that I may become more anxious about my risk for cancer based on these test results.

7 Alternatives: The alternative to genetic testing for cancer is to estimate my risk for cancer based on other known contributing causes, such as my age and pregnancy history.

8 Confidentiality: All information will be kept in strict confidence and anonymity by the staff handling the genetic testing work and results. My data has been assigned a code number which will be used instead of my name. This code number may be used for research and/or education purposes in all publications and/or scientific presentations so that identification by anyone other than the principal investigators will not be possible. The results of these studies will not be included in my medical record, and will not be available to any other parties, e.g., insurance companies. Before receiving my test results, I will have the choice of how I would want to be told of my results and with whom.

9 Screening and Treatment Issues: The possibilities for prophylactic surgery, screening and early detection for certain kinds of cancer will be explained to me. I will be given time to ask questions related to the benefits, risks, and limitations of these choices.

10 Access to Support Resources: I have been informed of the availability of a cancer genetics counselor, a specialist trained in the genetic assessment and counseling of individuals at genetic risk for cancer and/or undergoing genetic testing. This specialist will be familiar with making referrals to medical, psychological, and support resources to address issues and concerns as they arise prior and after I receive genetic test results. These support services will continue to be provided to me and my family, both immediately after I learn the results of my tests and in the months following, as needed.

11 Costs: The billing process for my participation in this study has been explained to me in the educational session. Since the identification of gene mutations related to cancer is still in the research stage, I will not be charged for the cost of these genetic tests. The counseling sessions with the cancer genetics counselor are free of charge, for as long as needed, but my insurance company will be billed for any clinic visits and for any exams that I have done. For exams done at Fox Chase Cancer Center, the Family Risk Assessment Program will take what my insurance company will pay and will not bill me for the remainder. If I have an HMO, I will obtain a referral from my primary physician. If I have a deductible associated with my insurance, I will be responsible for that. I will be responsible for covering the costs associated with any referrals made to me or my family member(s) for medical, psychological, and support care.

12 Withdrawal and Termination: Participation in this genetic research study is voluntary. I am free to withdraw my consent and discontinue participation in this genetic research study at any time without prejudice or effect to me or my family's present or subsequent medical care and access to genetic counseling. No genetic test results will be given to me without my permission. All information will remain and be kept in strict confidence and anonymity.

13 Compensation: There is no cost nor monetary reimbursement for my participation in this genetic counseling research study. Participation in this program does not include monetary reimbursement for any medical and psychological care, treatments, and/or tests generated outside of this genetic research study. I fully understand that if I suffer personal injury as a result of participation in this genetic counseling research study, no monetary compensation is or will be available for payment of my lost wages or other losses, including employment and insurance coverage losses.

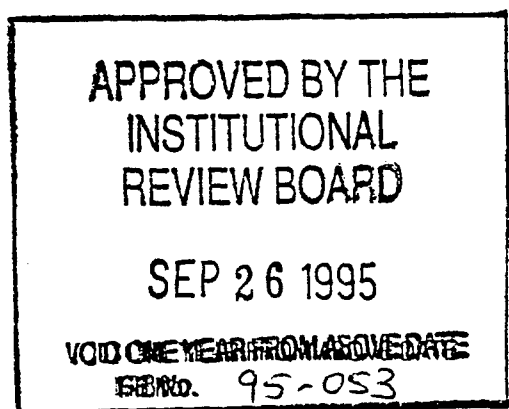
14 Voluntary Consent: If I am not satisfied with the manner in which this genetic research study is being conducted, I may report (anonymously if I so choose) any complaints to the Institutional Review Board by calling (215) 728-2931, 9:00 a.m. to 5:00 p.m., Monday to Friday, or by addressing a letter to the Institutional Review Board, in care of Lorraine B. Berger, Fox Chase Cancer Center, 7701 Burholme Avenue, Philadelphia, PA 19111. For additional questions concerning the research, I may contact the principal investigator listed above. By signing below, I indicate that I have read this form, received acceptable answers to my questions, and have agreed to participate in this genetic research study, as described above, to have my risk for carrying a cancer related gene assessed. I will receive and keep a copy of this form.

15 _____
Name of Participant

16 _____
Signature of Participant Date

17 I have explained the terms and conditions of the consent form of this research study to the above participant and based on this conversation, I believe he/she has understood what was discussed.

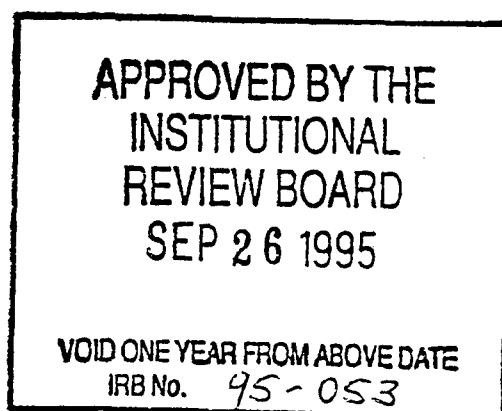
18 _____
Signature and title of witness to consent Date



19 **Addendum:** With this written consent, I give permission to Dr. Mary B. Daly and the team members of the Family Risk Assessment Program, who are a part of this research study, to provide any results of my personal risk for carrying a cancer related gene to the following person(s) upon their request. These persons may be members of my family, friends, physicians, clergy, and/or other.

| | | |
|----|-------|-----------------------------|
| 20 | _____ | _____ |
| | Name | Relationship to participant |
| 21 | _____ | _____ |
| | Name | Relationship to participant |
| 22 | _____ | _____ |
| | Name | Relationship to participant |
| 23 | _____ | _____ |
| | Name | Relationship to participant |

| | | |
|----|---------------------------------|-------|
| 24 | _____ | _____ |
| | Signature of Participant | Date |
| 25 | _____ | _____ |
| | Signature of Witness to consent | Date |



APPENDIX D

For office use only

ID # _____

MR # _____

Initial Visit _____ / _____ / _____

MM/DD/YY

Health History Questionnaire

Family Risk Assessment

This questionnaire has been developed by the Fox Chase Cancer Center in conjunction with the Fox Chase Network to collect information about your family history and your personal health. This information will help us identify medical or family history information that is important in understanding cancers that may run in a family. Participation is voluntary and you can withdraw at any time. All the information that you provide will be kept confidential. A code number will be used to track any information and your name will not be used. If you do participate, you will receive a family tree called a pedigree and feedback about your family history. Your participation will benefit you and your family by helping you better understand your risk for cancer. Please sign below, if you agree to participate in this Family Risk Assessment. Thank you.

Signature

Date

Section A -- Personal History

Name: _____

(first)

(middle)

(last)

(street)

Address: _____

(city)

(state)

(zip)

Telephone: Home () _____ Work () _____

1. What is your race or ethnic background?

1 ☐ White

2 ☐ Black

3 ☐ Hispanic

4 ☐ Asian

5 ☐ Other _____

2. What is the highest level of schooling you've completed?

1 ☐ Grade school

2 ☐ High school/G.E.D.

3 ☐ College

4 ☐ Post graduate

3. Which of the following describes your current marital situation?

1 ☐ Never married

2 ☐ Married or living as married

3 ☐ Divorced or separated

4 ☐ Widowed

SECTION B -- FAMILY HISTORY OF CANCER

Part 1 -- You, Your Spouse, Your Parents and Your Grandparents

- Fill in the full name, "Date of Birth" and "Date of Death" (where applicable) of each family member. Include only blood relatives and spouse. Do not include adoptive, foster or step- parents or grandparents. Circle "A" if the relative is alive and "D" if the relative is deceased.
- For each relative, circle whether or not they have had cancer. (Circle Yes or No). If you are not certain, circle "?" and fill in whatever information you can. **The shaded areas should only be completed for those relatives who have had cancer.**
- For those who have had cancer, fill in what type of cancer they have had -- "Type of Cancer," and about how old they were when they were told they had cancer "Age at Diagnosis." When possible, name the hospital where the cancer was treated and, if deceased, the place "City and State" of death.
- * If you are not certain of some dates of birth or dates of death, please estimate the year and circle those that are estimates.

| | First & Last Name | Date of Birth MM/DD/YY | Alive(A) Deceased(D) (circle) | Date of Death MM/DD/YY | Has had Cancer (circle) | Type of Cancer | Age at Diagnosis | Hospital Cancer was Treated | Place "City & State" of Death |
|----|-------------------|---------------------------|-------------------------------------|---------------------------|----------------------------|----------------|------------------|-----------------------------|-------------------------------|
| 1 | Yourself | ___/___/___ | A D | ___/___/___ | Yes No ? | _____ | _____ | _____ | _____ |
| 2 | Your Mother | ___/___/___ | A D | ___/___/___ | Yes No ? | _____ | _____ | _____ | _____ |
| 3 | Mother's Mother | ___/___/___ | A D | ___/___/___ | Yes No ? | _____ | _____ | _____ | _____ |
| 4 | Mother's Father | ___/___/___ | A D | ___/___/___ | Yes No ? | _____ | _____ | _____ | _____ |
| 5 | Your Father | ___/___/___ | A D | ___/___/___ | Yes No ? | _____ | _____ | _____ | _____ |
| 6 | Father's Mother | ___/___/___ | A D | ___/___/___ | Yes No ? | _____ | _____ | _____ | _____ |
| 7 | Father's Father | ___/___/___ | A D | ___/___/___ | Yes No ? | _____ | _____ | _____ | _____ |
| 8 | Spouse | ___/___/___ | A D | ___/___/___ | Yes No ? | _____ | _____ | _____ | _____ |
| 9 | _____ | ___/___/___ | A D | ___/___/___ | Yes No ? | _____ | _____ | _____ | _____ |
| 10 | _____ | ___/___/___ | A D | ___/___/___ | Yes No ? | _____ | _____ | _____ | _____ |

SECTION B -- FAMILY HISTORY OF CANCER

Part 2 -- Your Brothers and Sisters

- Fill in the full names, "Date of Birth" and "Date of Death" (where applicable) of your brothers and sisters. Include only blood relatives. Do not include adoptive, foster or step-brothers or sisters. Circle "B" for brother and "S" for sister. Include their "Date of Birth" and circle "A" if the relative is alive and "D" if the relative is deceased.
- For each relative, circle whether or not they have had cancer. (Circle Yes or No). If you are not certain, circle "?" and fill in whatever information you can. **The shaded areas should only be completed for those relatives who have had cancer.**
- For those who have had cancer, fill in what type of cancer they have had -- "Type of Cancer," and about how old they were when they were told they had cancer "Age at Diagnosis." When possible, name the hospital where the cancer was treated and, if deceased, the place "City and State" of death.
- * If you are not certain of some dates of birth or dates of death, please estimate the year and circle those that are estimates.

☐ Check here if you have no brothers or sisters.

office use
only

| First & Last Name | Brother or Sister | Date of Birth MM/DD/YY | Alive(A) Deceased(D) (circle) | Date of Death MM/DD/YY | Has had Cancer (circle) | Type of Cancer | Age at Diagnosis | Hospital Cancer was Treated | Place "City & State" of Death | |
|-------------------|-------------------|---------------------------|-------------------------------------|---------------------------|----------------------------|----------------|------------------|-----------------------------|-------------------------------|----------|
| 11 _____ | B S | ___/___/___ | A D | ___/___/___ | Yes No ? | _____ | _____ | _____ | _____ | HM HF |
| 12 _____ | B S | ___/___/___ | A D | ___/___/___ | Yes No ? | _____ | _____ | _____ | _____ | |
| 13 _____ | B S | ___/___/___ | A D | ___/___/___ | Yes No ? | _____ | _____ | _____ | _____ | |
| 14 _____ | B S | ___/___/___ | A D | ___/___/___ | Yes No ? | _____ | _____ | _____ | _____ | |
| 15 _____ | B S | ___/___/___ | A D | ___/___/___ | Yes No ? | _____ | _____ | _____ | _____ | |
| 16 _____ | B S | ___/___/___ | A D | ___/___/___ | Yes No ? | _____ | _____ | _____ | _____ | |

SECTION B -- FAMILY HISTORY OF CANCER

Part 3 -- Your Children

- Fill in the names, "Date of Birth" and "Date of Death" (where applicable) of your children. Include only blood relatives. Do not include adoptive, foster or step-children. Circle "S" for son and "D" for daughter. Circle "A" if the relative is alive and "D" if the relative is deceased.
- For each relative, circle whether or not they have had cancer. (Circle Yes or No). If you are not certain, circle "?" and fill in whatever information you can. **The shaded areas should only be completed for those relatives who have had cancer.**
- For those who have had cancer, fill in what type of cancer they have had -- "Type of Cancer," and about how old they were when they were told they had cancer "Age at Diagnosis." When possible, name the hospital where the cancer was treated and, if deceased, the place "City and State" of death.
- * If you are not certain of some dates of birth or dates of death, please estimate the year and circle those that are estimates.

☐ Check here if you have no biological children.

office use
only

| First & Last Name | Son or Daughter | Date of Birth MM/DD/YY | Alive(A) Deceased(D) (circle) | Date of Death MM/DD/YY | Has had Cancer (circle) | Type of Cancer | Age at Diagnosis | Hospital Cancer was Treated | Place "City & State" of Death |
|-------------------|-----------------|---------------------------|-------------------------------------|---------------------------|----------------------------|----------------|------------------|-----------------------------|-------------------------------|
| 17 _____ | S D | ____/____/____ | A D | ____/____/____ | Yes No ? | _____ | _____ | _____ | _____ |
| 18 _____ | S D | ____/____/____ | A D | ____/____/____ | Yes No ? | _____ | _____ | _____ | _____ |
| 19 _____ | S D | ____/____/____ | A D | ____/____/____ | Yes No ? | _____ | _____ | _____ | _____ |
| 20 _____ | S D | ____/____/____ | A D | ____/____/____ | Yes No ? | _____ | _____ | _____ | _____ |
| 21 _____ | S D | ____/____/____ | A D | ____/____/____ | Yes No ? | _____ | _____ | _____ | _____ |
| 22 _____ | S D | ____/____/____ | A D | ____/____/____ | Yes No ? | _____ | _____ | _____ | _____ |

SECTION B -- FAMILY HISTORY OF CANCER

Part 4 -- Your Mother's Brothers and Sisters

- Fill in the names, "Date of Birth" and "Date of Death" (where applicable) of your mother's brothers and sisters. Include only blood relatives. Do not include adoptive, foster or step- brothers or sisters. Circle "B" for brother and "S" for sister. Include their "Date of Birth" and circle "A" if the relative is alive and "D" if the relative is deceased.
- For each relative, circle whether or not they have had cancer. (Circle Yes or No). If you are not certain, circle "?" and fill in whatever information you can. **The shaded areas should only be completed for those relatives who have had cancer.**
- For those who have had cancer, fill in what type of cancer they have had -- "Type of Cancer," and about how old they were when they were told they had cancer "Age at Diagnosis." When possible, name the hospital where the cancer was treated and, if deceased, the place "City and State" of death.
- If you are not certain of some dates of birth or dates of death, please estimate the year and circle those that are estimates.

☐ Check here if your mother had no brothers or sisters.

office use
only

| First & Last Name | Brother or Sister | Date of Birth MM/DD/YY | Alive(A) Deceased(D) (circle) | Date of Death MM/DD/YY | Has had Cancer (circle) | Type of Cancer | Age at Diagnosis | Hospital Cancer was Treated | Place "City & State" of Death |
|-------------------|-------------------|---------------------------|-------------------------------------|---------------------------|----------------------------|----------------|------------------|-----------------------------|-------------------------------|
| 23 | B S | / / | A D | / / | Yes No ? | | | | |
| 24 | B S | / / | A D | / / | Yes No ? | | | | |
| 25 | B S | / / | A D | / / | Yes No ? | | | | |
| 26 | B S | / / | A D | / / | Yes No ? | | | | |
| 27 | B S | / / | A D | / / | Yes No ? | | | | |
| 28 | B S | / / | A D | / / | Yes No ? | | | | |

SECTION B -- FAMILY HISTORY OF CANCER

Part 5 -- Your Father's Brothers and Sisters

- Fill in the names, "Date of Birth" and "Date of Death" (where applicable) of your father's brothers and sisters. Include only blood relatives. Do not include adoptive, foster or step- brothers or sisters. Circle "B" for brother and "S" for sister. Include their "Date of Birth" and circle "A" if the relative is alive and "D" if the relative is deceased.
- For each relative, circle whether or not they have had cancer. (Circle Yes or No). If you are not certain, circle "?" and fill in whatever information you can. **The shaded areas should only be completed for those relatives who have had cancer.**
- For those who have had cancer, fill in what type of cancer they have had -- "Type of Cancer," and about how old they were when they were told they had cancer "Age at Diagnosis." When possible, name the hospital where the cancer was treated and, if deceased, the place "City and State" of death.
- * If you are not certain of some dates of birth or dates of death, please estimate the year and circle those that are estimates.

☐ Check here if your father had no brothers or sisters.

office use
only

| First & Last Name | Brother or Sister | Date of Birth MM/DD/YY | Alive(A) Deceased(D) (circle) | Date of Death MM/DD/YY | Has had Cancer (circle) | Type of Cancer | Age at Diagnosis | Hospital Cancer was Treated | Place "City & State" of Death |
|-------------------|-------------------|---------------------------|-------------------------------------|---------------------------|----------------------------|----------------|------------------|-----------------------------|-------------------------------|
| 29 _____ | B S | ____/____/____ | A D | ____/____/____ | Yes No ? | _____ | _____ | _____ | _____ |
| 30 _____ | B S | ____/____/____ | A D | ____/____/____ | Yes No ? | _____ | _____ | _____ | _____ |
| 31 _____ | B S | ____/____/____ | A D | ____/____/____ | Yes No ? | _____ | _____ | _____ | _____ |
| 32 _____ | B S | ____/____/____ | A D | ____/____/____ | Yes No ? | _____ | _____ | _____ | _____ |
| 33 _____ | B S | ____/____/____ | A D | ____/____/____ | Yes No ? | _____ | _____ | _____ | _____ |
| 34 _____ | B S | ____/____/____ | A D | ____/____/____ | Yes No ? | _____ | _____ | _____ | _____ |

HM
HF

SECTION B -- FAMILY HISTORY OF CANCER

Part 6 -- Additional Family Members

- Please use this page to add any additional blood relations, such as first cousins, grandchildren, nieces or nephews who you think should be included in your family history.
- Fill in the name, "Date of Birth" and "Date of Death" (where applicable) of each relative. Include only blood relatives. Do not include adoptive, foster or step- relatives. Circle "M" for male and "F" for female. Circle "A" if the relative is alive and "D" if the relative is deceased.
- For each relative, circle whether or not they have had cancer. (Circle Yes or No). If you are not certain, circle "?" and fill in whatever information you can. **The shaded areas should only be completed for those relatives who have had cancer.**
- For those who have had cancer, fill in what type of cancer they have had -- "Type of Cancer," and about how old they were when they were told they had cancer "Age at Diagnosis." When possible, name the hospital where the cancer was treated and, if deceased, the place "City and State" of death.
- **If you are not certain of some dates of birth or dates of death, please estimate the year and circle those that are estimates.**

office use
only

| First & Last Name | Relationship | Male or Female (circle 1) | Date of Birth MM/DD/YY | Alive(A) Deceased(D) (circle) | Date of Death MM/DD/YY | Has had Cancer (circle) | Type of Cancer | Age at Diagnosis | Hospital Cancer was Treated | Place "City & State" of Death | REL # |
|-------------------|--------------|---------------------------|---------------------------|-------------------------------------|---------------------------|----------------------------|----------------|------------------|-----------------------------|-------------------------------|-------|
| 35 | | M F | / / / | A D | / / / | Yes No ? | | | | | |
| 36 | | M F | / / / | A D | / / / | Yes No ? | | | | | |
| 37 | | M F | / / / | A D | / / / | Yes No ? | | | | | |
| 38 | | M F | / / / | A D | / / / | Yes No ? | | | | | |
| 39 | | M F | / / / | A D | / / / | Yes No ? | | | | | |
| 40 | | M F | / / / | A D | / / / | Yes No ? | | | | | |

Section C -- Reproductive History

1. How old were you when your periods began? (____) Years old
2. Do you currently have menstrual periods?
 - 1 ☐ Yes *SKIP TO Q.5*
 - 2 ☐ No *CONTINUE*
3. If you are not still menstruating, how old were you when your periods stopped?
(____) Years old
4. If you are not still menstruating, why did your periods stop?
 - 1 ☐ Natural menopause
 - 2 ☐ Surgical hysterectomy
 - 3 ☐ Other _____
5. How many live born children have you had? (____)
 - a. With how many of your children did you breast-feed? (____)
 - b. In your lifetime, for how many total months did you breast-feed? (____) months
6. How many miscarriages have you had? (____)
7. How many terminated pregnancies (abortions) have you had? (____)
8. How old were you when your first child was born?
(____) Years old
9. In your opinion, have you ever had any problems in getting pregnant?
 - 1 ☐ Yes *CONTINUE*
 - 2 ☐ No *SKIP TO Q.10*
 - 8 ☐ Don't Know *SKIP TO Q.10*

a. If yes, how long did it take you to get pregnant? (____) Years

☐ Never got pregnant

b. Have you ever consulted a doctor about difficulty in getting pregnant?

1 ☐ Yes

2 ☐ No

c. If yes, what was the diagnosis of the problem?

DIAGNOSIS _____

10. Have you ever taken Clomid (Clomiphene) or Pergonal to induce ovulation?

1 ☐ Yes *CONTINUE*

2 ☐ No *SKIP TO Q.11*

a. For how many months was Clomid used?

1 ☐ 0 months

2 ☐ 1

3 ☐ 2-3

4 ☐ 4-5

5 ☐ 6-11

6 ☐ 12+ months

b. For how many months was Pergonal used?

1 ☐ 0 months

2 ☐ 1

3 ☐ 2-3

4 ☐ 4-5

5 ☐ 6-11

6 ☐ 12+ months

11. Have you ever used birth control pills?

1 ☐ Yes *CONTINUE*

2 ☐ No *SKIP TO Q.12*

a. If yes, how old were you when you started taking them? _____ years

b. If yes, for how many years did you use them? _____ years

12. Have you ever used hormone replacement medication (for example: Premarin)?

1 ☐ Yes *CONTINUE*

2 ☐ No *SKIP TO SECTION D*

3 ☐ Don't know *SKIP TO SECTION D*

a. If yes, for how many years did you use them? _____ years

Section D -- Exposures

1. Have you ever used products which contain talc (e.g. dusting power with talc)?

1 ☐ Yes
2 ☐ No
8 ☐ Don't know

2. Were you ever treated with a series of x-rays to the front of your neck for acne, neck tumor or any other reason? (This does not include routine screening x-rays like, dental, chest or mammograms).

1 ☐ Yes
2 ☐ No

3. How many alcoholic drinks do you consume per day?

1 ☐ None/Rarely
2 ☐ 0 - 1 per day
3 ☐ 2 per day
4 ☐ 3 - 4 per day
5 ☐ Greater than 4 per day

4. Have YOU smoked a cigarette, even a puff in the past 30 days?

1 ☐ Yes **GO TO PART 2**
2 ☐ No **(CONTINUE)**

5. Have you smoked 100 cigarettes in your lifetime? That's about 5 packs.

1 ☐ Yes **GO TO PART 1 BELOW**
2 ☐ No **SKIP TO SECTION E**

PART 1 -- FOR FORMER CIGARETTE SMOKERS ONLY

6. About how old were you when you first started smoking at least one cigarette per day? (____) years old

7. When you were smoking regularly, how many cigarettes did you smoke on a typical day? (____) cigarettes
not packs per day

8. About how old were you when you last quit smoking? (____) years old
9. For how many years did you smoke regularly, at least one cigarette a day? (____) years

SKIP TO SECTION E IF YOU COMPLETED PART 1 ABOVE

PART 2 -- FOR CURRENT CIGARETTE SMOKERS ONLY

10. About how old were you when you first started smoking at least one cigarette a day? (____) years old
11. For how many years have you smoked regularly, at least one cigarette a day? (____) years
12. Since you started smoking regularly, about how many cigarettes do you smoke on a typical day? (____) cigarettes
not packs per day
13. During the past 7 days, how many cigarettes did you smoke on a typical day? (____) cigarettes
not packs per day
14. Do you smoke your first cigarette during the first half hour (30 minutes) after you wake up?

- 1 ☐ Yes
2 ☐ No

Section E -- Personal Medical History

1. What is your weight now? _____ lbs.
2. What is your height now? _____ ft./in.
3. Have you ever had any of the following medical conditions? (*CIRCLE YES=1, NO=2, DON'T KNOW=8*)

| | <u>YES</u> | <u>NO</u> | <u>DON'T KNOW</u> |
|----------------------------|------------|-----------|-------------------|
| Endometriosis | 1 | 2 | 8 |
| Cysts on the ovaries | 1 | 2 | 8 |
| Fibrocystic breast disease | 1 | 2 | 8 |
| Rectal/colon polyps | 1 | 2 | 8 |
| Ulcerative colitis | 1 | 2 | 8 |
| Abnormal pap smear | 1 | 2 | 8 |

4. Please list any medicine you take on a regular basis. Please include _____ prescription and non-prescription drugs as well as vitamins.

5. Have you ever had a breast biopsy (that is when a sample of breast tissue is _____ taken and examined for abnormalities)?

- ☐ Yes **CONTINUE**
☐ No **SKIP TO Q.6**
☐ Don't know **SKIP TO Q.6**

a. If yes, how many breast biopsies have you had? _____ biopsies

6. Have you ever **considered** having your breasts surgically removed to prevent breast cancer? (This is called prophylactic mastectomy).

- ☐ Yes
☐ No

7. Have either or both of your breasts been removed?

- 1 ☐ Yes
 - a ☐ one *CONTINUE*
 - b ☐ both *CONTINUE*
- 2 ☐ No *GO TO Q.8*

a. If yes, why did you have your breast(s) removed?

- 1 ☐ I had breast cancer
- 2 ☐ To prevent my developing breast cancer
- 3 ☐ Other _____

8. Have you ever **considered** having your ovaries surgically removed to prevent ovarian cancer? (This is called prophylactic oophorectomy).

- 1 ☐ Yes
- 2 ☐ No

9. Have you ever had a hysterectomy (surgical removal of the uterus)?

- 1 ☐ Yes *CONTINUE*
- 2 ☐ No *CONTINUE*
- 8 ☐ Don't know *CONTINUE*

a. If yes, how old were you? (____) years

10. Have either or both of your ovaries been surgically removed?

- 1 ☐ Yes *CONTINUE*
 - a ☐ both
 - b ☐ one
- 2 ☐ No *SKIP TO SECTION F*
- 8 ☐ Don't know *SKIP TO SECTION F*

a. If yes, how old were you? (____) years

b. If yes, why did you have your ovaries removed?

- 1 ☐ I had ovarian cancer
- 2 ☐ To prevent my developing ovarian cancer
- 3 ☐ Other _____

Section F -- General Medical Care

1. Have you ever had a mammogram (an x-ray of the breasts)?

1 ☐ Yes *CONTINUE*
2 ☐ No *SKIP TO Q.2*

- a. If yes, how old were you when you had your first mammogram?

_____ years

- b. If yes, how many mammograms have you had in the past 5 years?

_____ mammograms

- c. When was the last time you had a mammogram? _____ (approximately)
Mo/Yr

- d. Have you ever been told that a mammogram you had was abnormal?

1 ☐ Yes
2 ☐ No

2. During the past 6 months, about how often did you examine your own breasts for lumps or other changes?

_____ times

3. When did a physician or a health care practitioner last examine your breasts?

1 ☐ Within the past year
2 ☐ Between one and three years ago
3 ☐ More than three years ago
4 ☐ Never

4. Have you ever had a Pap smear?

1 ☐ Yes *CONTINUE*
2 ☐ No *SKIP TO Q.5*

- a. If yes, when was the last time you had a Pap smear?

_____ (approximately)
Mo/Yr

5. Have you ever had any of the following tests to screen for ovarian cancer?

- a. Pelvic exam (examination of the cervix and uterus by a physician or health care practitioner)

1 ☐ Yes
2 ☐ No
8 ☐ Don't Know

If yes, how many pelvic exams have you had in the past 5 years? _____ exams

When was the last time you had this? _____ (approximately)
Mo/Yr

- b. CA-125 (a blood test that is sometimes used to find ovarian cancer)

1 ☐ Yes
2 ☐ No
8 ☐ Don't know

If yes, how many CA-125 tests have you had in the past three years?

_____ years

When was the last time you had this? _____ (approximately)
Mo/Yr

- c. Pelvic or transvaginal ultrasound

- In a pelvic ultrasound, a probe is moved over your abdomen to project sound waves and an image is displayed on a screen.
- A transvaginal ultrasound involves inserting a plastic sound probe into the vagina and an image of the ovaries is displayed on a screen.

1 ☐ Yes
2 ☐ No
8 ☐ Don't know

If yes, how many pelvic or transvaginal ultrasound exams have you had in the past five years? _____ (Don't include those done for pregnancy).

When was the last time you had this? _____ (approximately)
Mo/Yr

6. Have you ever had a test for blood in your stool (bowel movements)?

- 1 ☐ Yes
- 2 ☐ No
- 8 ☐ Don't know

7. Have you ever had a sigmoidoscopy or a colonoscopy? (Both exams involve using a thin, lighted tube to examine the colon and rectum).

- 1 ☐ Yes
- 2 ☐ No
- 8 ☐ Don't know

The next three questions ask your opinion about your chances of getting cancer someday.

8. In your opinion, what are your chances of getting breast cancer someday?

- 1 ☐ Much more than the average woman
- 2 ☐ More than the average woman
- 3 ☐ Same as the average woman
- 4 ☐ Less than the average woman
- 5 ☐ Much less than the average woman

9. In your opinion, what are your chances of getting ovarian cancer someday?

- 1 ☐ Much more than the average woman
- 2 ☐ More than the average woman
- 3 ☐ Same as the average woman
- 4 ☐ Less than the average woman
- 5 ☐ Much less than the average woman

10. In your opinion, what are your chances of getting colon cancer someday?

- 1 ☐ Much more than the average woman
- 2 ☐ More than the average woman
- 3 ☐ Same as the average woman
- 4 ☐ Less than the average woman
- 5 ☐ Much less than the average woman

11. What type of health insurance do you currently have?

- 1 ☐ Uninsured
- 2 ☐ Blue Cross/Blue Shield
- 3 ☐ Other private insurance _____
- 4 ☐ HMO... specify _____
- 5 ☐ Medicare
- 6 ☐ Medicaid

If you would like your doctor to be informed of our screening recommendations, please provide us with his/her name, address and telephone number below.

Name: _____

Address: _____

Phone: () _____

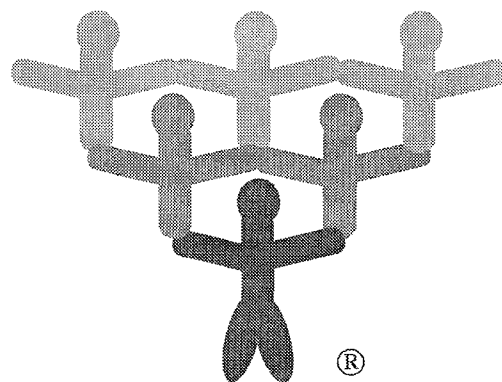
Thank you

| |
|----------------------------------|
| <i>For Office Use Only</i> _____ |
| _____ |
| _____ |
| _____ |

APPENDIX E

Family Cancer Risk Counseling Training for Nurses

May 16-18, 1995



Sponsored by Fox Chase Cancer Center and funded in part by the Department of Defense Infrastructure Grant (1994-1997) and the Oncology Nursing Foundation/Oncology Nursing Certification Corporation Education Research Grant (1994-1996).



FAMILIAL CANCER RISK COUNSELING

May 16 - 18, 1995

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APPENDIX

Listing of Regional Cancer Risk Screening Programs and
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Bibliography

Reprint: "Assessment and Counseling for Women with a Family History of Breast Cancer"

Post Test Questions

Program Evaluation





FAMILIAL CANCER RISK COUNSELING

May 16 - 18, 1995

Agenda

Day 1 - May 16, 1995

- | | |
|------------|---|
| 8:00 a.m. | Registration and Continental Breakfast |
| 8:30 a.m. | Welcome and Introduction - AGNES MASNY |
| 8:40 a.m. | Keynote Address - THERESA CONWAY Nursing in Cancer Genetics: A personal perspective. |
| 9:30 a.m. | Principles of Basic Genetics - JOSEPHINE WAGNER |
| 10:30 a.m. | Break |
| 10:45 a.m. | Molecular Genetics of Carcinogenesis - MARY DALY |
| 12:00 p.m. | Lunch |
| 1:00 p.m. | Overview of the Human Genome Project, Genetic Testing - KEN BUETOW |
| 2:00 p.m. | Break |
| 2:15 p.m. | Genetic Principles (cont'd) and Patterns of Mendelian Inheritance - JOSEPHINE WAGNER |
| 3:00 p.m. | Patterns of familial cancers Review of familial cancer pedigrees Activity |
| 4:30 p.m. | Wrap-up and homework |



Josephine Wagner, BS, MS

Principles of Basic Genetics

Objectives

At the end of this sessions, the nurse will be able to:

1. Demonstrate familiarity with terms used in the field of genetics.
2. Describe how genetic terms are used in the realm of cancer genetics.
3. Identify the three common patterns of Medellian Inheritance.

Principles of Basic Genetics

Presentation

- A. Review of Genetic terminology
 - 1) Definitions associated with chromosomes
 - a) aneuploidy
 - b) chromosomal aberrations
 - 2) Definitions associated with genes
 - a) alleles
 - b) exon
 - c) intron
 - 3) Definitions associated with DNA
 - a) base pairs
 - b) mutations.
- B. Recognizing Patterns of Mendelian Inheritance
 - 1) Degrees of relation
 - a) first degree, relative to the client
 - b) second degree, relative to the client
 - c) third degree, relative to the client
 - 2) autosomal dominant
 - 3) autosomal recessive
 - 4) chromosomal
 - 5) multifactorial, polygenic, non-Mendelian
 - 6) New germ-line (sporadic)
 - 7) examples of each.

Glossary of Genetics Terms

Adenine: A nitrogenous base, one member of the base pair A-T (*adenine-thymine*)

Allele: One of the alternative versions of a gene that may occupy a given locus on a chromosome.

Amplification: The production of multiple identical copies of a DNA sequence.

Aneuploidy: The occurrence of an additional or missing chromosome to give an unbalanced chromosome complement (e.g., trisomy, monosomy).

Anticipation: The term used to denote the progressively earlier appearance and increased severity of a disease in successive generations. It is thought to result from bias of ascertainment.

Ascertainment: The method of selection of individuals for inclusion in a genetic study.

Autosome: Any nuclear chromosome other than the sex chromosomes, X and Y; there are 22 pairs of autosomes in the human karyotype.

Base pair (bp): A pair of complementary nucleotide bases, as in double-stranded DNA. It is used as the unit of measurement of the length of a DNA sequence.

Bayesian analysis: A mathematical method widely used in genetic counseling to calculate recurrence risks. The method combines information from several sources (genetics, pedigree information, and test results) to determine the probability that a specific individual might develop or transmit a certain disorder.

Candidate gene: A gene suspected as being the gene mutated in a disorder, during molecular studies.

Carrier: An individual heterozygous for a particular (often mutant) allele. The term is used for heterozygotes for autosomal recessive alleles, for females heterozygous for X-linked alleles, or less commonly, for an individual heterozygous for an autosomal dominant allele but not expressing it, e.g., a heterozygote for the Huntington disease allele in the presymptomatic (before showing signs) state.

Centromere: The portion of the chromosome joining the two chromatids and separating the long and short arms of the chromosome.

Chromatid: A single DNA strand of a dividing chromosome, joined to its "sister chromatid" at the centromere.

Chromatin: The composite of DNA and proteins that make up the structure of a chromosome.

Chromosome: A highly ordered structure composed mainly of chromatin that resides in the nucleus of eukaryotic cells. The human genome consists of 46 chromosomes: 22 pairs of autosomes, and 1 pair of sex chromosomes.

Chromosomal disorder: A clinical condition caused by an abnormal chromosome constitution in which there is extra or missing chromosome material (either a whole chromosome or a chromosome segment).

Chromosomal instability syndromes: These syndromes exhibit increased DNA breakage due to carcinogen exposure and a decreased ability to repair broken or damaged DNA. This causes an increased number of DNA breakage to be passed to daughter cells which may result in cancer initiation.

Clinical heterogeneity: The production of clinically different phenotypes from mutations in the same gene.

Clone: An identical copy of a DNA sequence (or cell); "to clone" means to isolate a specific DNA sequence or gene.

Concordant: In human genetics, a twin pair in which both members exhibit the same certain trait.

Consanguinity: Relationship by descent from a common ancestor, for example, marriage between two first cousins.

Cytogenetics: The study of human chromosomes and their abnormalities.

Deletion: The loss of a sequence of DNA from a chromosome. The deleted DNA may be of any length from a single base to a large part of a chromosome.

Discordant: In human genetics, a twin pair of which one member shows a certain trait and the other does not. Not the same.

DNA sequence: The relative order of base pairs within the genome. The number of base pairs is often used as a measure of length of a DNA segment, for example, a 500 base pair sequence of a gene A was deleted in this blood sample tested.

DNA: Called deoxyribonucleic acid. It is the polymeric, double-stranded molecule that encodes genetic information that is transmitted from one generation to the next generation. The strands are held together by hydrogen bonds between nitrogenous bases that constitute the code adenine (A) and thymine (T), which pair with each other, and guanine (G) and cytosine (C), which pair with each other.

Dominant: The expressed gene, when the two genes of any pair are different alleles and only one is expressed, i.e., it requires only one altered copy to show itself.

Duplication: Presence of an additional copy of part of a chromosome or of a gene.

Empiric risk: The probability that trait will occur or recur in a family, based on past experience (statistics, epidemiology) rather than on knowledge of the mechanism(s) that caused that trait to happen.

Exon: A transcribed region of a gene that is present in mature messenger RNA, that codes for a protein. This is the region molecular geneticists look at for mutations when doing a genetic test.

First degree relative: Proband's parent, child, or sibling.

Gene: The unit of inheritance, consisting of a DNA sequence coding for a specific protein or component of a protein, arranged in a linear manner on chromosomes.

Genotype: The genetic makeup of an individual, either overall or for the trait(s) of particular interest.

Germ line: The cell lineage resulting in eggs or sperm.

Haplotype: A set of closely linked genes that tends to be inherited as a unit.

Heterogeneity: Phenomenon of multiple etiologies for the same (or very similar) conditions. The heterogeneity may involve different genetic mechanisms, as well as nongenetic causes.

Heterozygote: An individual with two different alleles at a particular locus on a chromosome.

Heritability: The proportion of variance of a characteristic due to genetic rather than environmental factors.

Homozygote: An individual with identical alleles at a particular locus on a chromosome.

Insertion: Viral insertion. Oncogenes were first discovered within viruses. Viral exposures have been implicated in about 5% of human cancers. Examples are hepatomas linked to Hepatitis B and cervical cancers due to papilloma viruses.

Intron: The DNA sequences in a gene that are not converted into messenger RNA, and which separate the coding regions (exons).

Inversion: The turning around of a chromosomal segment with consequent alteration of its fine structure and sometimes its function.

Karyotype: The chromosome constitution as displayed by a microscopic preparation of dividing chromosomes.

Linkage: The occurrence of two genetic loci close enough on the same chromosome to interfere with independent assortment at cell division.

Locus: The specific site of a gene on a chromosome.

Meiosis: The process of cell division leading to formation of eggs and sperm, with halving of the chromosome number.

Mendelian: Transmission of genes and resultant traits or disorders according to specific patterns and proportions as put forth by Gregor Mendel. Disorders transmitted in this manner are also referred to as "single-gene" disorders.

Mitosis: The process of cell division of somatic cells, in which the daughter cells are normally genetically identical to the parent.

Multifactorial: A type of inheritance used to describe traits or characteristics that are determined by a combination of genetic factors (i.e., many genes) influenced by an unknown or known environmental factor or factors.

Mutation: A permanent, heritable change from the normal to an altered form of a particular gene.

New-germline mutation: When a genetic test shows that a person is a carrier of a gene mutation which has not been inherited by either parent, i.e., it happened by chance during oogenesis or spermatogenesis.

Oncogene: A dominantly acting gene that induces uncontrolled cell growth and proliferation leading to tumor development.

p: The short arm of a chromosome.

Penetrance: Used to define the phenotype of a particular genotype. Penetrance can be full (100%) or low (less than 100%). For example, a carrier of a mutation in the Huntington's disease gene has a 100% chance of developing that condition, ie., full penetrance. A carrier of a mutation in the BRCA1 gene has an up to 85% chance of developing breast cancer. Therefore this gene mutation is not fully penetrant, because there will be 15% of BRCA1 carriers not developing breast cancer.

Phenotype: The visible expression of the action of a particular gene; the clinical picture resulting from a genetic disorder.

Polygenic/multifactorial: Determined by multiple genes and usually also by non-genetic factors.

Polymerase chain reaction (PCR): A technique in which a short DNA or RNA sequence can be amplified, even from a single cell; a very potent molecular DNA diagnostic tool.

Proband: Individual who first brings a family to attention for genetic evaluation and counseling; also called the index case or propositus.

Probe: A term used in a molecular genetics lab to describe a sequence of DNA or RNA that is labeled with a radioactive molecule and used to locate (recognize) similar sequences within a person's genome (genetic make-up).

q: The long arm of a chromosome.

Recessive: A trait or gene that is expressed only if the individual is homozygous for a given allele.

Recombination: The separation of alleles that are close together on the same chromosome by crossing over of homologous chromosomes at meiosis.

RFLP - Restriction fragment length polymorphism: Inherited variation in DNA detected by the cutting of DNA at different points by a restriction enzyme. Can be used for diagnosis when linked to a mutant gene in a family.

RNA: Also called ribonucleic acid. It is like DNA (deoxyribonucleic acid) except that RNA has ribose (a sugar) instead of deoxyribose in its backbone. It is made up of adenine, cytosine, guanine, and uracil instead of thymine.

Robertsonian translocation: The formation of a single abnormal chromosome by the joining of two chromosomes by their short arms.

Second degree relative: Proband's grandparent, grandchild, aunt, uncle, niece, nephew or half-sibling.

Somatic: Involving the body cells rather than the germ line.

Suppressor gene: A regulatory gene which functions in controlling normal cell growth; a mutation can permit unregulated cell growth leading to cancer.

Third degree relative: Proband's first cousins, great-grandparent, great-grandchild, great-uncles and aunts, great-nieces and nephews, and half-aunts, uncles, nieces, and nephews.

Thymine: A nitrogenous base, one member of the base pair A-T (adenine-thymine)

Translocation: Transfer and exchange of genetic material between different chromosomes, not members of the same pair. A translocation is balanced when no chromosome material is lost or gained in the rearrangement.

Tumor suppressor gene: Growth-suppressing genes which play an important role in the regulation of cell growth. Loss of both copies of a tumor suppressor gene results in deregulated growth and potentially a neoplasm.

X-linked: The genes and the conditions that are determined by the genes on the X chromosome are said to be X-linked. Some of conditions determined on the X chromosome are: Fragile X, several types of color blindness, several types of deafness, Hemophilia A and B, Lesch-Nyhan Syndrome, and Becker's muscular dystrophy.

References

Portions of the glossary text were taken directly or modified from definitions in the following:

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Familial Cancer Risk Counseling Training
May 16, 1995

Post-Session Evaluation

Principles of basic genetics

| | | | |
|--|------------|-------------|----------------------|
| 1. To what extent did this session meet the stated objectives? | not at all | somewhat | completely met |
| a. the nurse will be able to demonstrate familiarity with terms used in the field of genetics | | | |
| b. the nurse will be able to describe how genetic terms are used in the realm of cancer genetics | | | |
| c. the nurse will be able to identify three common patterns of Mendelian Inheritance | | | |
| 2. Please rate the teaching effectiveness of the presenter. | not at all | somewhat | completely effective |
| 3. Please rate the relevance of this session to the overall course goal: to provide nurses with the knowledge and skills necessary to provide genetic cancer risk information. | not at all | somewhat | completely relevant |
| 4. Please rate this session for its level of appropriateness for training nurses in Familial Cancer Risk Counseling | too basic | appropriate | too detailed |
| 5. Would you recommend that this session be included in future training programs for Familial Cancer Risk Counseling? | yes | no | |

Please offer any suggestions for future training sessions

Molecular Genetics of Carcinogenesis

Objectives

Upon completion of the class, the nurse will be able to:

1. Explain the genetic basis of Carcinogenesis
2. Describe the stages of carcinogenesis and genetic manifestations.
3. Understand how molecular genetic concepts apply to risk estimation.

Molecular Genetics of Carcinogenesis

Presentation

A. Carcinogenesis

1. Definition
2. Process
3. Causes
 - a. chemical
 - b. physical
 - c. biologic
 - d. genetic
4. Stages of Carcinogenesis
 - a. initiation
 - b. promotion
 - c. progression

B. Genetic Basis of Carcinogenesis

1. Types of Mutations
2. Cancer Cytogenetics
3. Oncogenes
4. Tumor Suppressor Genes
5. Mismatch Repair Genes

- C. Molecular epidemiology of Cancer
 - 1. Host Factors
 - 2. Exposure Factors
 - 3. Gene-Environment Interactions
 - 4. Implications for Risk Assessment
 - 5. Colon Cancer - a Model.

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Molecular Genetics of Carcinogenesis

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Familial Cancer Risk Counseling Training
May 16, 1995

Post-Session Evaluation

Molecular Genetics of Carcinogenesis

| | | | |
|--|------------|-------------|----------------------|
| 1. To what extent did this session meet the stated objectives? | not at all | somewhat | completely met |
| a. the nurse will be able to explain the genetic basis of carcinogenesis | | | |
| b. the nurse will be able to describe stages of carcinogenesis and genetic manifestations | | | |
| c. the nurse will be able to understand how molecular genetic concepts apply to risk estimation | | | |
| 2. Please rate the teaching effectiveness of the presenter. | not at all | somewhat | completely effective |
| 3. Please rate the relevance of this session to the overall course goal: to provide nurses with the knowledge and skills necessary to provide genetic cancer risk information. | not at all | somewhat | completely relevant |
| 4. Please rate this session for its level of appropriateness for training nurses in Familial Cancer Risk Counseling | too basic | appropriate | too detailed |
| 5. Would you recommend that this session be included in future training programs for Familial Cancer Risk Counseling? | yes | no | |

Please offer any suggestions for future training sessions

Overview of the Human Genome Project, Genetic Testing

Objectives

Upon completion of the class, the nurse will be able to:

1. Describe the objectives of the human genome project.
2. List at least 3 techniques used in genetic testing.
3. Explain the benefits and limitations of genetic testing for cancer susceptibility.

Overview of the Human Genome Project and Genetic Testing

Presentation

A. Introduction

- 1) Genetics and risk
 - a) susceptibility paradox - we know what causes disease, but don't know who will develop disease
 - b) differences in genetic constitutions may resolve paradox
 - c) breast cancer pedigree
 - d) Dungeons and Dragons example

B. The Human Genome Initiative

- 1) Building the infrastructure for human genetics
 - a) goals of the Genome Project
 - b) levels of biologic resolution
- 2) Different types of genome maps and their level of resolution
 - a) the genetic map of the human genome
 - b) the "physical" map of the human genome
 - c) the sequence of the human genome
- 3) What can we expect to see in the near future
 - a) all of the genes identified (tagged) - within 1 year
 - b) a complete "physical" map - within 3 years
 - c) a "preliminary" sequence - within 5 years
- 4) What are the implications?

C. Applying the tools of genetics to Risk Counseling

- 1) Genetic testing - background
 - a) historical perspective
 - b) genetic testing in medicine/society
 1. transfusion/organ transplant
 2. paternity/forensics
 - c) routine part of prenatal counseling/pediatrics
- 2) Genetic testing - what is it?
 - a) DNA sample
 1. blood
 2. buccal swab
 3. other
 - b) Laboratory Protocol
 1. PCR
 2. gel electrophoresis
 3. DNA sequencing
 - c) Example: testing for p53 mutations
- 3) Genetic testing - application in Cancer Risk Counseling
 - a) high risk families
 1. linkage screening
 2. mutation screening
- 4) Genetic testing - the future
 - a) molecular pathology
 - b) chemotherapy
 - c) chemoprevention
 - d) behavioral interventions
- 5) Genetic testing - caveat emptor
 - a) polymorphism versus mutations
 - b) we can only test for the "current" paradigm
 - c) the issue of confidentiality
 - d) predisposition is NOT predestination.

Familial Cancer Risk Counseling Training
May 16, 1995

Post-Session Evaluation

Overview of the Human Genome Project and Genetic Testing

| | | | |
|--|------------|-------------|----------------------|
| 1. To what extent did this session meet the stated objectives? | not at all | somewhat | completely met |
| a. the nurse will be able to describe the objectives of the human genome project | | | |
| b. the nurse will be able to list at least 3 techniques used in genetic testing | | | |
| c. the nurse will be able to explain benefits and limitations of genetic testing for cancer | | | |
| 2. Please rate the teaching effectiveness of the presenter. | not at all | somewhat | completely effective |
| 3. Please rate the relevance of this session to the overall course goal: to provide nurses with the knowledge and skills necessary to provide genetic cancer risk information. | not at all | somewhat | completely relevant |
| 4. Please rate this session for its level of appropriateness for training nurses in Familial Cancer Risk Counseling | too basic | appropriate | too detailed |
| 5. Would you recommend that this session be included in future training programs for Familial Cancer Risk Counseling? | yes | no | |

Please offer any suggestions for future training sessions

Josephine Wagner, BS, MS

Inherited Patterns of Cancer

Objectives

At the end of this sessions, the nurse will be able:

1. To identify criteria for sporadic, familial, and hereditary patterns of cancer
2. To list at least three familial cancer syndromes associated with common cancers.
3. To construct a basic cancer family pedigree.

Inherited Patterns of Cancer

Course Outline

A. Sporadic Cancer Family Histories

- 1) New germ-line occurrences
- 2) examples of sporadic cancer family histories

B. Familial Cancer Family Histories

- 1) multifactorial, polygenic , non-Mendelian
- 2) examples of sporadic cancer family histories

C. Hereditary Pre-Neoplastic Cancer Family Syndromes

- 1) chromosomal instability disorders
 - a) Ataxia-Telangiectasia
 - b) Xeroderma Pigmentosa
- 2) genodermatoses (ie., with skin involvement)
 - a) Basal Cell Nevus Syndrome (Gorlin Syndrome)
 - b) Dysplastic Nevus
- 3) immunodeficiency syndromes
 - a) Wiskott-Aldrich
- 4) phacomatoses (ie., affecting central nervous system)
 - a) Neurofibromatosis, type I
 - b) von Hippel-Lindau

D. Hereditary Cancer Family Syndromes

- 1) Breast
 - a) examples of pedigrees
- 2) Ovary
 - a) examples of pedigrees
- 3) Colon
 - a) examples of pedigrees
- 4) other
 - a) examples of pedigrees

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Familial Cancer Risk Counseling Training
May 16, 1995

Post-Session Evaluation

Inherited Patterns of Cancer

| | | | |
|--|------------|-------------|----------------------|
| 1. To what extent did this session meet the stated objectives? | not at all | somewhat | completely met |
| a. to identify criteria for sporadic, familial, and hereditary patterns of cancer | | | |
| b. the nurse will be able to list at least 3 familial cancer syndromes associated with common cancer | | | |
| c. the nurse will be able to construct a basic cancer family pedigree | | | |
| 2. Please rate the teaching effectiveness of the presenter. | not at all | somewhat | completely effective |
| 3. Please rate the relevance of this session to the overall course goal: to provide nurses with the knowledge and skills necessary to provide genetic cancer risk information. | not at all | somewhat | completely relevant |
| 4. Please rate this session for its level of appropriateness for training nurses in Familial Cancer Risk Counseling | too basic | appropriate | too detailed |
| 5. Would you recommend that this session be included in future training programs for Familial Cancer Risk Counseling? | yes | no | |

Please offer any suggestions for future training sessions



FAMILIAL CANCER RISK COUNSELING

May 16 - 18, 1995

Agenda

Day 2 - May 17, 1995

- | | |
|------------|---|
| 8:00 a.m. | Continental Breakfast |
| 8:30 a.m. | Questions and Answers - AGNES MASNY, JOSEPHINE WAGNER, and RICKY PRESTON |
| 8:45 a.m. | Obtaining and Interpreting Client's History - RICKY PRESTON |
| 9:45 a.m. | Activity: Case presentation: - RICKY PRESTON and JOSEPHINE WAGNER |
| 10:45 a.m. | Break |
| 11:00 a.m. | Familial Cancer Risk Information - AGNES MASNY |
| 12:00 p.m. | Lunch |
| 1:00 p.m. | Nursing Role in Providing Familial Cancer Risk Information - AGNES MASNY |
| 2:00 p.m. | Break Out Session I - Case presentation and role play |
| 3:00 p.m. | Break |
| 3:15 p.m. | Break Out Session II - Case presentation and role play |
| 4:15 p.m. | Group discussion of cases - Questions and Answers |



Obtaining and Interpreting Family History Information

Objectives

Upon completion of the class, the nurse will be able to:

1. Identify key areas to be covered in a health history.
2. Explain the importance of confirming a cancer diagnosis in a client's relative.
3. Describe strategies for dealing with some behavioral challenges in the history taking of a client who suspects a genetic predisposition to cancer.
- D. Begin to formulate process for incorporating clear, concise history taking into practice.

Obtaining and Interpreting Client's History

Presentation

A. Client History

Function:

- 1) Gather data/establish a data base
- 2) Learn about a real or potential illness (Risk Assessment)
- 3) Individualize treatment/follow up recommendations
- 4) Establish a relationship

Structure:

- 1) Identifying data
 - a) Age
 - b) Sex
 - c) Race/Ethnicity
 - d) Occupation
- 2) Referral source/reliability
- 3) Chief complaint or reason for seeking care
- 4) Present illness/concern
- 5) Past medical history
- 6) Past surgical history
- 7) Current health status

ETOH

Tobacco

Diet

Exercise

Allergies

Medications (including OTC)

Safety measures

Health Maintenance Activities

Environmental exposures

- 8) Family history (usual is two generations for genetic risk assessment obtain data on three generations)
 - a) Age
 - b) Sex
 - c) Medical problems
 - d) Genetic disorders
 - e) Age and cause of death
- 9) Psychosocial History
 - a) Support systems
 - b) Perceptions/concerns
 - c) Depression/anxiety
- 10) Review of Systems (see separate sheet)
Extent of the ROS depends on the reason for the visit, the client's age, sex and risk factors.

Setting the stage for the History:

- 1) Review the client's medical record if available
- 2) Provide an environment conducive to history taking
 - a) Private
 - b) Respectful of names/titles
 - c) Promptness
 - d) Seating patterns
- 3) Note taking
 - a) Explain reason
 - b) Brief/precise
 - c) Avoid during discussion of sensitive issues YOU WON'T FORGET!
- 4) Communication Skills
 - a) Follow patient leads (but stay focused)
 - b) Never assume
 - c) Be empathetic
 - d) Use direct questions
 - e) Ask one question at a time
 - f) Avoid medical terminology
 - g) Always end with asking client if there is anything else they wish to discuss.
- 5) Behavioral Challenges - Clients may present the following during history taking:
 - a) Overtalkative client
 - b) Client with multiple concerns
 - c) Angry client
 - d) Depressed client
 - e) Anxious client
 - f) Client with confusing history/poor historian

B. Family History

Purpose:

- 1) Gather data
- 2) Formulate cancer risk assessment
- 3) Client education
- 4) Individualize cancer screening guidelines.

Method:

- 1) Client completes family history questionnaire prior to session and questionnaire is expanded/clarified during session
- 2) Initial history is obtained during session.

Who to include: The maternal and paternal extended nuclear family needs to be included. This includes all first degree and second degree relatives; children, parents, siblings, grandparents, aunts, uncles and cousins.

Information to be obtained includes:

- 1) Family members who have had cancer:
 - a) cancer site/primary and metastasis
 - b) unilateral vs. bilateral
 - c) number of primaries
 - d) pathological diagnosis
 - e) age at diagnosis
 - f) date of diagnosis
 - g) place of diagnosis
 - h) name when diagnosed
 - i) current age or age at death
 - j) environmental exposures
- 2) Family members without a cancer diagnosis (current or past)
 - a) current age
 - b) if deceased, age and cause of death
 - c) participation in cancer screening activities
- 3) Client/Proband
If with a cancer diagnosis:
 - a) current age
 - b) presence of physical findings associated with certain inherited forms of cancer (benign skin moles, familial polyposis)
 - c) participation in cancer screening activities
 - d) presence of other non-inherited cancer risk factors
 - e) reproductive history

If client has had a cancer diagnosis, do 1-5 plus

 - f) information, re: cancer dx

| | |
|--------------------|--------------------------------|
| Type of cancer | Treatment(s) |
| Age at diagnosis | Follow-up recommendations |
| Place of diagnosis | Physician(s) involved in care. |

C. Confirming the Diagnosis

- 1) Obtain permission from the affected relative (if deceased, ask next of kin)
- 2) Confirm with other family members
- 3) Obtain pathology report
- 4) Obtain hospital records
 - a) Physician notes
 - b) Discharge summary
 - c) Autopsy report
 - d) Death certificate

D. Focus Areas for Family History

- 1) Number of relatives with same or related cancers
- 2) Ages at cancer diagnosis
- 3) Autosomal dominant pattern
- 4) Familial clustering of rare cancers
- 5) Multifocal or bilateral cancers
- 6) Multiple primary cancers in same individual
- 7) Decrease/absence of environmental risks
- 8) Presence of physical findings suspicious for hereditary cancer syndrome.

HELPFUL HINTS IN OBTAINING FAMILY HISTORY

1. Write down all relatives' names.
Refer to each relative individually.
2. Be aware initial history may be incomplete
3. Obtain written permission to obtain medical records and/or speak to other family members
4. Obtain names under which cancer diagnosis was made to facilitate record procurement
5. Elicit family involvement in completing history
6. Avoid getting involved in family dynamics!

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Familial Cancer Risk Counseling Training
May 17, 1995

Post-Session Evaluation

Obtaining and Interpreting Family History Information

| | | | |
|--|------------|-------------|----------------------|
| 1. To what extent did this session meet the stated objectives? | not at all | somewhat | completely met |
| a. the nurse will be able to identify key areas to be covered in a health history | | | |
| b. the nurse will be able to explain the importance of confirming a cancer diagnosis in a client's relative | | | |
| c. the nurse will be able to describe strategies for dealing with some of the challenges in taking a family history | | | |
| d. the nurse will begin to formulate a process for incorporating history taking into practice | | | |
| 2. Please rate the teaching effectiveness of the presenter. | not at all | somewhat | completely effective |
| 3. Please rate the relevance of this session to the overall course goal: to provide nurses with the knowledge and skills necessary to provide genetic cancer risk information. | not at all | somewhat | completely relevant |
| 4. Please rate this session for its level of appropriateness for training nurses in Familial Cancer Risk Counseling | too basic | appropriate | too detailed |
| 5. Would you recommend that this session be included in future training programs for Familial Cancer Risk Counseling? | yes | no | |

Please offer any suggestions for future training sessions

Familial Cancer Risk Information

Objectives

Upon completion of this class on Familial Cancer Risk Information, the nurse will be able to:

1. Describe the various risk models used in epidemiologic studies and in cancer risk assessment These risk models include: relative risk, absolute risk, cumulative risk, and family history (pedigree evaluation) as function in risk estimation.
2. Explain the benefits and limitations of risk models used in estimating an individual's risk for cancer.
3. Describe how cumulative risk models can be utilized in familial cancer risk counseling.

Familial Cancer Risk Information

I. Background Information regarding Risk (Offit & Brown, 1994; Schneider, 1994; Pennsylvania Department of Health, 1993; Peterson & Sims, 1993)

A. Causation - the necessary and sufficient factors for an outcome to occur

1. Logical Causation

- a. the factor must be present for an outcome to occur
- b. the factor is all that is required for the outcome to occur

2. Causation in medicine and health

- a. outcome may be linked to numerous factors
- b. causation can be inferred, i.e. the presence of factors increase likelihood that an outcome will occur.

B. Risk - term used to quantify the chance that some event will occur given the presence of some other factor. (important to remember that risk figures are estimates and not predictions)

1. Absolute risk - the proportion of disease in a defined group with a risk factor, relative to the total population with the risk factor)

- a. There is a 10% population risk of developing breast cancer, i.e., being female is a risk factor for breast cancer. One out of eight women will develop breast cancer reflects the absolute risk.

2. Relative risk - proportion of disease among those exposed (having a risk factor) relative to the proportion of disease in the unexposed (without the risk factor)

- a. the magnitude of risk can vary depending of the type of study and disease
- b. Relative risk of >1.0 increased risk in the exposed compared to persons without the risk. For example women with atypical hyperplasia on breast biopsy are 3.5 times more likely to develop breast cancer than women without hyperplasia.
- c. the risks are not cumulative. From the above example, you cannot say that women with atypia have 3.5 times the 10% population breast cancer risk, equalling a total of 30.5% risk
- d. Relative risks above 4 or 5 are viewed as more meaningful. Although risk ratios are useful for epidemiologic research, they present problems translating risk in the clinical setting (See Table 1. for selected risk ratios).

Table 1. Selected Risk Ratios for breast, ovarian and colon cancer

| Relative Affected | Risk Ratio |
|--|------------|
| Breast cancer (10% lifetime risk) | |
| Mother (any age) | 1.7-4.0 |
| Sister (any age) | 2-3 |
| Sister, premenopausal | 3.6-5.0 |
| Sister, postmenopausal | 2 |
| Sister, bilateral, early onset | 11 |
| Sister and mother | 2.5-14 |
| Sister and mother, premenopausal, bilateral breast | 39 |
| Second degree relative | 1.4-2.0 |
| Third degree relative | 1.35 |
| Ovarian cancer (1.4% lifetime risk) | |
| One first degree relative | 3.9-4.0 |
| Multiple cases (≥ 2) | 5.0-35 |
| Colon cancer (2.4% lifetime risk) | |
| Mother or father | 3.0-4.0 |
| Brother or Sister | 3.0-7.0 |
| First degree relative (FDR) | |
| with adenomatous polyp | 3.0-4.0 |
| FDR, age <60 with polyp | 3.6 |
| FDR, age >70 with polyp | 1.4 |
| Family history of colon ca proband with polyp | 3.0 |

Adapted from: "Female Reproductive Tract: Cervix, Endometrium, Ovary". by M. Daly, M. Bookman, & C. Lerman (1995). in Cancer Prevention and Control, (Eds.) Greenwald, Kramer, & Weed, NY: Marcel & Dekker pp. 598; and "Quantifying Familial Cancer Risk" (1994). by K. Offit & K. Brown in Journal of Clinical Oncology, 12(8), pp. 1725

C. Risk Perception (Lerman, Daly, et al., 1994; Palmer & Sainfort, 1993; Russell, 1993)

1. Factors that increase perception of risk
 - a. Severity of risk/level of adversity - impact of disease increases perception of risk
 - b. Proximity of risk - the closer to home the worse it is viewed
 - c. Degree of control - less voluntary control viewed as greater risk
 - d. Amount of publicity/education
 - e. Perceived susceptibility with increased cancer worriers
2. Giving risk factors and risk information often does not change the perception of risk

II. Risk Models

A. Cumulative Risk - models of analysis that allow for predication of cumulative risk for breast cancer at specific ages based on specific variables (See Table 2.)

Table 2. Cumulative Risk (%) for Individuals with FDRs with Cancer of Breast, Colon or Ovary, Compared with Individuals Having No Family History

| <u>Breast Cancer</u> | | | Individuals Having No Family Hx |
|----------------------|-----------------------------------|-------|------------------------------------|
| Age | Age of Affected Relative 30-39 | 60-69 | |
| 29 | .5 | .2 | .02 |
| 39 | 1.7 | .6 | .45 |
| 49 | 4.4 | 1.8 | 1.6 |
| 59 | 8.6 | 4.0 | 2.9 |
| 69 | 13.0 | 7.0 | 4.6 |
| 79 | 16.5 | 9.6 | 7.3 |

| <u>Colon Cancer</u> | | | Individuals Having No Family Hx |
|---------------------|----------------------------------|-----|------------------------------------|
| Age | Age of Affected Relative < 55 | ≥55 | |
| 29 | - | - | - |
| 39 | .2 | .1 | 0.0 |
| 49 | .9 | .5 | .1 |
| 59 | 2.8 | 1.0 | .6 |
| 69 | 5.0 | 2.2 | 1.3 |
| 79 | 8.4 | 4.4 | 2.4 |

| <u>Ovarian Cancer</u> | | | Individuals Having No Family Hx |
|-----------------------|-------------------------------|--|------------------------------------|
| Age | All Ages of Affected Relative | | |
| 29 | .25 | | - |
| 39 | .50 | | .1 |
| 49 | .50 | | .4 |
| 59 | 1.0 | | .5 |
| 69 | 3.0 | | 1.0 |
| 79 | 4.7 | | 1.2 |

From: "Quantifying Familial Cancer Risk" (1994). by K. Offit & K. Brown in Journal of Clinical Oncology, 12(8), pp. 1725.

1. Claus model (Claus, Risch, & Thompson, 1994) - to predict risk for women with a family history for breast cancer using the following variables.
 - family history on maternal and paternal side (same lineage)
 - age of onset of disease

Claus model (con't)

- a. advantages - presents cumulative risks based on age group. Is helpful in families with moderate risk (familial patterns).
- b. disadvantages - This model is based on a genetic model which may change as we learn more about BRCA1 and BRCA2 mutations. Therefore it may underestimate risk in BRCA1 and BRCA2 carriers and overestimate risk in families who are not carriers.

2. Gail Model - cumulative risk model using following variables:

- age at menarche, age at first live birth, number of first degree relatives with breast cancer, number of previous breast biopsies, current age of proband.

- a. advantages - allows more accurate prediction of risk in women undergoing yearly screening without a significant family history
- b. disadvantages - model does not take into account age of onset and second degree relatives. Therefore it may underestimate risk of genetic mutations from paternal side.

3. LOD score - Logarithm of Odds of Linkage

- a. statistical measure of the probability for linkage
- b. used in Linkage analysis, need a genetic statistician

4. Risk based on genetic testing

- a. genetic screening for cancer is not available commercially
- b. mutation screening is being done in the context of research
- c. where testing is conducted it is recommended that it be done
 - (1) where there is extensive experience in DNA-based diagnosis
 - (2) with counseling regarding the risks and benefits of testing and with information about the accuracy of the tests
- d. when mutation carriers will be identified risk estimates based on carrier status can be given
 - (1) for BRCA1 carrier - 85% to 90% estimated lifetime risk of breast cancer

5. Risk based on family history - prediction of risk is based on how the family appears to fit known hereditary cancer patterns

- a. having the same risk for cancer as the general population. Those individuals that appear to have a sporadic family cancer pattern.
- b. moderate risk/familial pattern
 - (1) less significant family history of cancer, not seen in each generation and older or average age of onset of disease

Table 3. Selected hereditary and cancer syndromes of cancer predisposition

| Syndrome | Associated Malignancies | Other clinical Manifestations |
|--------------------------------------|---|---|
| Breast cancer | Breast and ovarian Site-specific breast | |
| Cowden's disease | Breast, colon and thyroid cancers | multiple hamartomas, vitiligo, angiomas benign proliferative disease of multiple organs |
| Breast cancer in LiFraumeni | soft tissue sarcoma, breast, osteosarcoma, leukemia, brain tumors adrenocortical carcinoma | |
| Ataxia telangiectasia | breast, ovary, leukemia leukemia, lymphoma, GI cancer, brain tumors | autosomal recessive disorder with cerebral ataxia & nystagmus, oculocutaneous telangiectasia, varying degree of immunodeficiency, and sensitivity to ionizing radiation |
| Ovarian cancer | Breast and ovarian Site-specific ovarian | |
| Gorlin's disease | Basal cell carcinoma, brain tumor and ovarian | basal cell nevi |
| Familial adenomatous polyposis (FAP) | colorectal cancer | > 100 adenomas in the colon and rectum usually before age 20 |
| Lynch I | colorectal cancer | |
| HNPCC or Lynch II | colon, ovarian, and GI cancer (stomach, pancreas, biliary tree) | |
| Gardner's syndrome | colorectal cancer, and uncommonly are medullary thyroid carcinoma and hepatoblastomas | colonic polyposis and extraintestinal soft tissue tumors, osteomas, supernumerary teeth and retinal hypertrophy of the pigmentation epithelium |
| Muir-Torre Syndrome | GI tract, skin, GU system; benign breast and malignant tumors | |
| Peutz-Jeghers Syndrome | GI tract, breast, uterus ovary, and testis | abnormal melanin deposits, GI polyposis |

Adapted from: "Quantifying Familial Cancer Risk" by K. Offit & K. Brown. (1994). Journal of Clinical Oncology, 12(8), pp. 1726-1726; and "Assessment and counseling of women with a family history of breast cancer" by K.F. Hoskins, J.E. Stopfer, K.A. Calzone, S.D. Merajver, T.R. Rebbeck, J.E. Garber, and B.L. Weber. (1995) Journal of the American Medical Association, 273(7), pp. 582

Table 4. Risk Factors for Breast, Ovarian and Colon Cancers

| <u>Breast</u> | <u>Ovarian</u> |
|--|---|
| Age (>60 yrs) | Age (> 55 yrs) |
| Family History | Family History |
| Nulliparity | Nulliparity and/or infertility |
| Early onset of menarche (<12 years) | Never having used oral contraceptives |
| Age of first live birth (>30 yrs of age) | Chronic talc exposure |
| Proliferative atypical hyperplasia | high lactose intake, low galactotransferase |
| Postmenopausal obesity | |
| Women having had repeat fluoroscopy | |
| Alcohol intake (>1 drink per day) | |
| High fat intake (>38% calories from fat) | |
| Oral contraceptive use (use for over 10 yrs) | |
| <u>Colon</u> | |
| Age (>50 yrs) | |
| Family History | |
| colorectal adenomas | |
| colorectal cancer | |
| High total fat intake | |
| Low fiber intake | |
| Inflammatory bowel disease | |
| Chronic ulcerative colitis | |
| Chronic granulomatous colitis | |
| Family history of associated hereditary syndromes (Table 3.) | |

From: "Early Detection and Prevention of Breast Cancer" by K.J. Helzlsouer, pp. 512; "Female Reproductive Tract: Cervix, Endometrium, Ovary" by M. Daly, M. Bookman, & C. Lerman, pp 598; and "Prevention and Control of Colorectal Cancer" by S. Winawer & M. Shike. All in Cancer Prevention and Control. (1995) Greenwald, P., Krammer, B.S., & Weed, D.L. New York: Marcel Dekker.

- (2) may represent combined genetic and environmental effect
- (3) may have a dominant susceptibility gene with low penetrance, i.e. there seems to be higher rates of cancer than general population but not as significant as hereditary cancer pattern
- (4) may have an inherited cancer but due to limited family history it does not appear significant

c. high risk/putative hereditary pattern

- (1) multiple cases of cancer - 3 or more and often 2 FDRs
- (2) appears each subsequent generation (following autosomal dominant pattern)
- (3) cancers occur early - usually < 50 yrs.
- (4) fit hereditary cancer syndromes (See Table 3.)
- (5) bilaterality in paired organs

6. Role of gene/environment interaction

- a. cancer is multifactorial in nature
- b. all gene mutations do not have 100% penetrance. This means that even mutation carriers may not develop cancer.
- c. non-carriers of germline mutations still have potential risk to develop cancer
- d. must be aware of other risk factors (See Table 4.)

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** *highly recommended reading*

Familial Cancer Risk Counseling Training
May 17, 1995

Post-Session Evaluation

Familial Cancer Risk Information

| | | | |
|--|------------|-------------|----------------------|
| 1. To what extent did this session meet the stated objectives? | not at all | somewhat | completely met |
| a. the nurse will be able to describe the risk models used in cancer risk assessment | | | |
| b. the nurse will be able to explain benefits and limitations of risk models | | | |
| c. the nurse will be able to describe how cumulative risk models can be used in cancer risk counseling | | | |
| 2. Please rate the teaching effectiveness of the presenter. | not at all | somewhat | completely effective |
| 3. Please rate the relevance of this session to the overall course goal: to provide nurses with the knowledge and skills necessary to provide genetic cancer risk information. | not at all | somewhat | completely relevant |
| 4. Please rate this session for its level of appropriateness for training nurses in Familial Cancer Risk Counseling | too basic | appropriate | too detailed |
| 5. Would you recommend that this session be included in future training programs for Familial Cancer Risk Counseling? | yes | no | |

Please offer any suggestions for future training sessions

Nursing Role in Providing Familial Cancer Risk Information

Objectives

Upon completion of this class on the Nursing Role in Providing Familial Cancer Risk Information, the nurse will:

1. Have successfully demonstrated (through role play) collecting family history information, develop and assess a family pedigree, and provide preliminary risk information to a surrogate proband.
2. Describe the factors that influence risk perception.
3. Understand nursing responsibilities in providing cancer risk counseling.

Nursing Role in Providing Familial Cancer Risk Information

Introduction

Genetic mutations for cancer will continue to be isolated; rapidly moving medicine into the genetic era. Due to the limited numbers of genetic counselors knowledgeable about cancer nation-wide, oncology nurses will be called upon to provide cancer genetic information.

- I. International Society of Nurses In Genetics (ISONG) - members committed to maintaining a high standard of professional integrity in fostering the integration of genetic principles into the nursing process and delivery of genetic health care services.

II. Cancer genetic health care

A. Genetic Services

- 1. Identifying and referring individuals
- 2. Providing and managing comprehensive care which includes state of the art genetic screening, diagnosis, counseling and therapy
- 3. Evaluating and improving genetic health care capabilities
- 4. Educating individuals and families about genetics
- 5. Assessing and deliberating ethical, legal and social consequences of new and existing genetic services

- B. Genetic nursing is a clinical specialty which focuses on providing health care to clients at risk for known genetic conditions (Cancers caused or influenced by genes).

- 1. Standards in Genetic Nursing (ISONG, 1994)

- a. Collection and examination of genetic health data
- b. Identification of expected client outcomes
- c. Development, implementation and evaluation of plan of care based on current research

2. Roles and functions

- a. health promotion
- b. genetic screening and evaluation with referral for more specialized testing and evaluation when indicated
- c. direct care
- d. coordination of comprehensive care
- e. genetic counseling and education
 - (1) clarification of genetic information as understood by the client
 - (2) provision of objective genetic information to clients at risk
 - (3) reinforcement of counseling provided by other health professionals
- f. psychosocial support

3. Standards of Clinical Nursing Practice (ANA Social Policy Statement) as part of Familial Cancer Risk Counseling

- a. Assessment - a continuous process of collecting data about the client's health status, strengths and concerns. A comprehensive assessment includes information from variety of sources including:
 - (1) individual, family community, physical assessment and laboratory testing

(2) nursing activities - history taking to identify those at risk

(3) assessing the individual's understanding of risk

(a) Factors that increase perception of risk

- Severity of risk/level of adversity - impact of disease increases perception of risk
- Proximity of risk - the closer to home the worse it is viewed
- Degree of control - less voluntary control viewed as greater risk
- Amount of publicity/education
- Perceived susceptibility with increased cancer worriers

(b) Giving risk factors and risk information often does not change the perception of risk

- dispel myths where you can
- listen to individuals' understanding of risk

b. Diagnosis - categorizing patient behavior patterns including signs and symptoms. This can also include diagnosis regarding risk.

***** Risk diagnosis made as part of multi-disciplinary team and not given until cancers have been confirmed.*****

d. Planning and implementation - include the activities that the will be performed by the nurse, the client or others.

e. Evaluation - ongoing process

- (1) continued assessment of knowledge
- (2) impact of risk information
- (3) adherence to screening recommendations

4. Providing Risk Information

a. Sporadic Cancer Family Pattern

(1) Give risk category - probability of developing cancer is the same as the general population

(2) Explain limitations

- (a) cancer may have happened by chance
- (b) due to small or incomplete family history, the case appears to be sporadic

(3) Assess Client Understanding

b. Moderate Risk or Familial Cancer Pattern

(1) give risk category - pattern suggests that there may be something hereditary

- (a) can use empiric risk tables to compare the degree of increased risk
** use caution and know from which study the estimates are derived **

(2) Explain limitations

- (a) cancer may be multifactorial in nature
- (b) there may be a hereditary pattern but the gene has low penetrance
- (c) small or incomplete family history makes the family pattern appear less striking
- (d) breast cancer and colon cancer are common cancers. In large families they may appear striking but may be unrelated to inherited factors
- (e) if using empiric risk tables, remember these are estimates

(3) Assess client understanding

c. Hereditary Pattern

(1) give risk category - pattern suggests that the cancer is following a hereditary pattern

- (a) the proband has a 50% chance of inheriting a mutated gene. This represents the chance of inheriting the cancer susceptibility gene. This is different from the chance of developing a malignancy.
- (b) the lifetime risk of developing a breast or ovarian cancer for a BRCA1 carrier is 85 to 90%; and the risk of developing a colon cancer for a Lynch II carrier is 85 to 90%. Important to emphasize that this is risk of disease and not risk of death.
- (c) risk to offspring

(2) explain limitations

- (a) there is an 85% lifetime risk of developing a cancer but a 15% chance

that a cancer will not occur.

(3) assess client understanding

5. Genetic Testing - not commercially available at present.

a. testing being done in context of research

b. research protocol

(1) pre-test counseling prior to results

(2) post-test counseling

(3) follow-up

American Oncologic Hospital
Initial Visit Evaluation

Occupation:
Religion:

Ethnicity:

Birth Defects:

Exposures:
Tobacco-
Ethanol-

DATE: _____
HISTORY:

Cardiovascular-

Respiratory-

GI-

Neuro/Psych-

Musculo Skeletal-

Metabolic/Endocrine-

Skin-

GYN: Menarche: Periods:

G P A

LMP: Menopause:

Hormone Use: Last PAP:

Breast: Last Mammo:

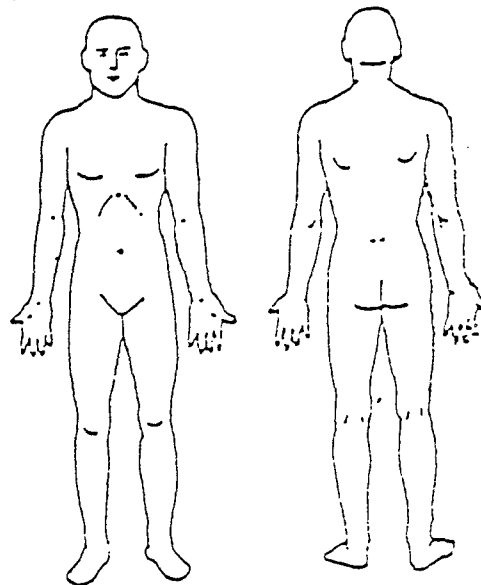
Previous Breast Biopsy:

SIGNATURE: _____

NAME: _____
PATIENT #: _____
AGE: _____ D.O.B. _____
HEIGHT: FT. _____ IN. _____ TEMP _____
WEIGHT: _____ LBS. WBC _____
HCT _____

Surface Area: _____ mc2 PLT _____

Physical Exam: _____



ALLERGY:

MEDICINES:

OPERATIONS:

SERIOUS MEDICAL ILLNESSES:

FAMILY HISTORY:

Maternal-

Paternal-

Sibs-

Children-

Familial Cancer Risk Counseling Training
May 17, 1995

Post-Session Evaluation

Nursing Role in Providing Familial Cancer Risk Information

| | | | |
|--|------------|-------------|----------------------|
| 1. To what extent did this session meet the stated objectives? | not at all | somewhat | completely met |
| a. the nurse will be able to describe the factors that influence risk perception | | | |
| b. the nurse will understand nursing's responsibility in providing cancer risk counseling | | | |
| c. the nurse will demonstrate (through role playing) the provision of familial cancer risk information | | | |
| 2. Please rate the teaching effectiveness of the presenter. | not at all | somewhat | completely effective |
| 3. Please rate the relevance of this session to the overall course goal: to provide nurses with the knowledge and skills necessary to provide genetic cancer risk information. | not at all | somewhat | completely relevant |
| 4. Please rate this session for its level of appropriateness for training nurses in Familial Cancer Risk Counseling | too basic | appropriate | too detailed |
| 5. Would you recommend that this session be included in future training programs for Familial Cancer Risk Counseling? | yes | no | |

Please offer any suggestions for future training sessions



FAMILIAL CANCER RISK COUNSELING

May 16 - 18, 1995

Agenda

Day 3 - May 18, 1995

- | | |
|------------|--|
| 8:00 a.m. | Continental Breakfast |
| 8:30 a.m. | Overview for Day Questions and Answers |
| 8:45 a.m. | Medical Management and Surveillance: The Role of the Oncology Team - MARY DALY |
| 9:45 a.m. | Break |
| 10:00 p.m. | Psychosocial Impact of Cancer Risk - JUDITH MUCH |
| 11:00 a.m. | Brunch |
| 12:00 p.m. | Ethical and Legal Implications of Genetic Screening - COLLEEN SCANLON |
| 1:00 p.m. | Panel - Issues and Implications for Establishing Cancer Risk Assessment Services Nursing - PAT HERMAN Medical - JENNY GRANA Administrative - TRACY JONES |
| 2:30 p.m. | Break |
| 2:45 p.m. | Wrap-Up Post-test Evaluation Scheduling of Preceptorship dates |



Medical Management and Surveillance

Objectives

Upon completion of the class, the nurse will be able to:

1. Describe surveillance strategies for individuals having increased risk for a familial cancer.
2. Discuss the advantages and limitation of prophylactic surgery.
3. Discuss the role of the nurse as part of the oncology team:
in managing medical surveillance.

Medical Management and Surveillance:
The Role of the Oncology Team

Presentation

A. Team Members

1. Physician
2. Nurse - Educator
3. Genetic Counselor
4. Social Worker
5. Psychologist

B. Team Responsibilities

1. Identification of High Risk Individuals
2. Education
3. Risk Assessment
4. Preventive Recommendations
 - a. primary
 - b. secondary

C. Surveillance of Germline Mutation Carriers

1. Breast
2. Ovary
3. Colon

D. Support issues

1. Family Issues
2. Psychological Support
3. Social Implications
4. Public Health issues.

//

Colon Cancer Screening Recommendations

1.

| Screening Procedure | Frequency | Comments/ Familial Risk Category |
|--|--|--|
| Fecal occult blood testing (FOBT) and digital rectal examination | <u>Average risk</u> - FOBT annually starting at age 40. | <p><u>Personal history of a sporadic breast or gynecologic cancer</u>, in the absence of family history of other malignancies.</p> <p><u>HNPCC or Lynch II</u> - - "Amsterdam criteria"</p> <p>a. At least 3 relatives with history of colorectal or other cancers, especially adenocarcinomas of the endometrium, stomach, pancreas, and biliary tree, as well as transitional cell cancers of the genitourinary tract. One member of the kindred must be a first degree relative.</p> <p>b. Affected members in at least two generations</p> <p>c. At least one affected individual being < 50.</p> <p>* Patients in families with HNPCC or Lynch II should be referred for gynecologic exam.</p> |
| Flexible sigmoidoscopy (FS) | <p><u>Average risk</u> - FS annually starting at age 50, then every 3-5 years if normal.</p> <p><u>Personal history of sporadic breast or gynecologic cancer</u> - same as the average risk, except that FS screening begins as soon as a breast or gyn cancer is diagnosed. Do not wait till 50 to begin FS.</p> | |
| Colonoscopy | <p><u>Hereditary Non-Polyposis Colon Cancer (HNPCC) or Lynch II (Family Cancer Syndrome)</u></p> <p>Survey all family members of an affected kindred with FOBT and rectal exam, then colonoscopy beginning at age 5 years younger than the earliest age of development of colon CA in the family or at the age of 20 if this is unknown.</p> <p>Annual colonoscopy until no adenomas, then frequency decreased to every 2-3 years.</p> | |

FOX CHASE
CANCER CENTER

Colon Cancer Screening Recommendations

2.

| Screening Procedure | Frequency | Comments/Familial Risk Category |
|-----------------------------|---|---|
| Flexible Sigmoidoscopy (FS) | <p><u>Familial Adenomatous Polyposis (FAP)</u></p> <ul style="list-style-type: none"> ◆ annual FS beginning at age 12 until polyps are found, then begin annual colonoscopy. ◆ FS with polypectomies every 4-12 months when multiple adenomas found and subtotal colectomy and proctectomy done. | <p><u>Familial Adenomatous Polyposis</u></p> <ul style="list-style-type: none"> ◆ Upper endoscopy should be done when colorectal adenomas are identified, and repeated every two years. ◆ When multiple adenomas are found, prophylactic colectomy should be performed (by age 30). ◆ If proctocolectomy done, there is no need for further GI evaluation. |
| Colonoscopy | <p><u>Family history of sporadic colorectal cancer</u></p> <ul style="list-style-type: none"> ◆ Colonoscopy beginning at age ten years less than affected family member, or at age 40 (whichever comes first), then every 5 years until two consecutive normal studies, then as for average risk. <p><u>Personal history of colorectal cancer</u></p> <ul style="list-style-type: none"> ◆ Full colonoscopy at 6 & 12 months post-resection (with biopsies of anastomotic line), repeat annually for 4 more years, then every 3 years. ◆ FOBT and rectal exam annually when interval between colonoscopies > 1 year. ◆ CEA every 6 months x 3 then annually for five years | <p><u>Family history of sporadic colorectal cancer</u></p> <ul style="list-style-type: none"> ◆ Single first degree relative with colon cancer (2-4 fold increased risk). ◆ More than one first degree relative (FDR), same surveillance as for one FDR. ◆ If > 2 FDRs, look for other evidence of HNPCC. |

Colon Cancer Screening Recommendations

3.

| Screening Procedure | Frequency by disease category |
|---------------------|--|
| Colonoscopy | <p><u>History of Removal of an Adenomatous polyp</u></p> <ul style="list-style-type: none"> Single or a small number of adenomatous polyps: colonoscopy every 3 years until no more polyps, then colonoscopy every 5 years. Some patients with multiple adenomas or with suboptimal clearance of all polyps, may need repeat colonoscopy within 1 year, then re-evaluate. Single small tubular adenoma, can follow-up with colonoscopy in 5 years. <p><u>Ulcerative Colitis (UC)</u> (1% of all colorectal cancers)</p> <ul style="list-style-type: none"> Ulcerative proctitis - same as average risk. Left-sided colitis - colonoscopies every 1-2 years beginning 12-15 years after diagnosis, with biopsies every 10 cm. Best done when colitis is inactive (dysplasia can be confused with acute inflammatory changes). <p>Low grade dysplasia - treat UC aggressively and repeat colonoscopy in 3-6 months, or consider prophylactic proctocolectomy.</p> <p>High grade dysplasia (or if low-grade dysplasia persists on repeat biopsies) strongly consider proctocolectomy.</p> <p><u>Universal or pan colitis</u></p> <ul style="list-style-type: none"> Same as left-sides UC, but begin colonoscopies after 8 years of disease. <p><u>Crohn's disease</u> (risk increased 7 to 20 fold)</p> <ul style="list-style-type: none"> Begin screening after 10 years of disease: Colonoscopy every 2 years, biopsies of any stricture, polyp, nodule, fistula, or any suspicious lesions. Small bowel must be surveyed for cancer in long- standing ileal Crohn's. |

Breast Cancer Screening Recommendations

The following screening recommendations are made for women with a family history of breast cancer in a first or second degree relative. For clients with a family history of early onset breast cancers, initiation of screening is recommended 10 years earlier than the earliest age of onset of a first or second degree relative.

| Screening Procedure | Frequency | Comments/Familial Risk Category |
|-----------------------------------|---|---|
| Breast self-exam (BSE) | Monthly from age 20. | <u>Site specific Breast Cancer</u> <ul style="list-style-type: none">♦ Breast cancer at any age with first degree relative (FDR) or 2 or more second degree relatives. <u>Hereditary Breast and Ovarian Cancer</u> <ul style="list-style-type: none">♦ Ovarian cancer at any age, with a FDR with ovarian cancer at any age, or a first degree relative with breast cancer before 50 years.♦ Relative with primary breast and ovarian cancers.♦ Sister pair both with breast or ovarian cancer. |
| Clinical Breast Examination (CBE) | CBE every 6 to 12 months depending on physical findings and quality of mammograms. May recommend CBE every 6 months for women with dense breasts and non-revealing mammograms or for women with heightened anxiety due to risk. | |
| Mammography | For women under 35 years, initiation of mammography is recommended 10 years earlier than earliest onset of breast cancer, then repeat annually depending on quality. Annually for women 35 and over. For suspicious findings not referred for ultrasound, repeat in 6 months. | |

Ovarian Cancer Screening Recommendations

The following screening recommendations are made for women with a family history of ovarian cancer in at least one first degree relative, two or more second degree relatives or a family history of ovarian cancer and multiple cancer, i.e., breast, colon, or other Lynch II cancers (See colon cancer screening recommendations). In early onset ovarian cancers, initiation of screening is recommended 10 years earlier than the earliest age of onset.

| Screening Procedure | Frequency | Comments/Familial Risk Category |
|--|---|---|
| Pelvic Examination | At baseline and then repeat every 6 months | <p><u>Site Specific Ovarian Cancer</u></p> <ul style="list-style-type: none"> ♦ Ovarian cancer at any age with a first degree relative (FDR) or 2 or more second degree relatives. ♦ Having at least one affected FDR increases the life-time risk (OR = 3.6) <p><u>Hereditary Breast and Ovarian Cancer</u></p> <ul style="list-style-type: none"> ♦ Ovarian cancer at any age, with a FDR with ovarian cancer at any age, or a first degree relative with breast cancer before 50 years. ♦ Relative with primary breast and ovarian cancers. ♦ Sister pair both with breast or ovarian cancer. <p><u>Ovarian Cancer with HNPCC or Lynch II</u></p> <ul style="list-style-type: none"> ♦ Ovarian cancer approximately 20 years earlier than general population. ♦ Family clustering of ovarian, colon, endometrial, small bowel, stomach, pancreas, and transitional cell carcinoma of ureter and renal pelvis. <p>**Families with ovarian and HNPCC or Lynch II cancers should be referred for gastro-enterologic exam.</p> <p><u>Personal history of ovarian cancer</u></p> <ul style="list-style-type: none"> ♦ Follow screening recommendations for breast cancer |
| CA -125 | <p>At baseline, repeat in 6 months and then annually to alternate with transvaginal ultrasound</p> <ul style="list-style-type: none"> ♦ Normal range: 8-35 U/ml ♦ Elevation >35 U/ml rule out pregnancy, endometriosis, or other cancer. If no other cause, repeat in 2 to 3 months. ♦ Transvaginal ultrasound with two successive elevated levels. | |
| Transvaginal Ultrasound with combination of pulsed Doppler | <p>At baseline and then repeat annually.</p> <ul style="list-style-type: none"> ♦ Premenopausal women are scheduled during the follicular phase of the menstrual cycle. ♦ Repeat scanning if questionable. ♦ Surgical exploration if suspicious. | |

Medical Management and Surveillance:
The Role of the Oncology Team

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Familial Cancer Risk Counseling Training
May 18, 1995

Post-Session Evaluation

Medical Management and Surveillance

| | | | |
|--|------------|-------------|----------------------|
| 1. To what extent did this session meet the stated objectives? | not at all | somewhat | completely met |
| a. the nurse will be able to describe cancer surveillance strategies for high risk individuals | | | |
| b. the nurse will be able to discuss the advantages & disadvantages of prophylactic surgery | | | |
| c. to describe the role of the nurse as part of the oncology team in managing surveillance | | | |
| 2. Please rate the teaching effectiveness of the presenter. | not at all | somewhat | completely effective |
| 3. Please rate the relevance of this session to the overall course goal: to provide nurses with the knowledge and skills necessary to provide genetic cancer risk information. | not at all | somewhat | completely relevant |
| 4. Please rate this session for its level of appropriateness for training nurses in Familial Cancer Risk Counseling | too basic | appropriate | too detailed |
| 5. Would you recommend that this session be included in future training programs for Familial Cancer Risk Counseling? | yes | no | |

Please offer any suggestions for future training sessions

Psychosocial Impact of Cancer Risk Information

Objectives

Following the presentation, the nurse will be able to:

1. List four (4) common emotional reactions of clients to cancer risk information.
2. Discuss how to introduce the need for a referral to mental health professional to the client.
3. Name an emotional reaction to cancer risk information and describe the counseling response.

Psychosocial Impact of Cancer Risk

Presentation

- A. Introduction
- B. What motivates some one to seek counseling in the first place?
 - 1) Realistic concerns
 - 2) New service
 - 3) Relative with a problem
 - 4) Emotional insurance policy
 - 5) Unrealistic expectations.
- C. Why pay attention to feelings?
 - 1) What we have learned from other risk counseling models.
 - a) General
 - 1. Genetic counseling is a potential crisis experience that can be either beneficial or harmful.
 - 2. Do not blunt emotions.
 - 3. Don't focus on emotions at expense of information sharing, but can't give information if there are emotional barriers to communication.
 - 4. Emotionals and psychological needs are understandable only within the context of overall life experience/history.
 - b) AIDS
 - 1. Much & Cotteta - individuals, regardless of educational background, etc., lose all rational perspective when counseling is needed secondary to perceived exposure.
 - 2. Provide as much information as possible prior to crisis point or diagnostic visit, as individual may be unable to hear during that time of anxiety.
 - c) Huntington's
 - 1. Biesecker, et al., - what is different between Huntington's and hereditary susceptibility to breast cancer is that with breast cancer screening and intervention may reduce morbidity and mortality in mutation carriers.
 - 2. Wiggins, et al., - in Huntington's those individuals who go informative results, regardless of content (anything but indeterminate) got a positive psychological benefit from counseling.
 - 3. Kessler - generally the difference currently (until testing becomes much easier) between utilizers and non-utilizers of predictive testing is "ego-strength" - relatively good self-concept, better developed interpersonal skill, and better able to tolerate anxiety.

4. Huggins, et al. - may want to redefine what good and bad news is if person has defined him/herself in term of a disease, if they find out they do not have it, adjustment may be just as difficult as if they do - "survivor guilt."
5. Bloch, et al. - point out the ripple effect in families even though testing is a decision made only by the effected party him/herself - counseling must also be available for the family.
6. Block, et al. (1993) - model of stages of response to predictive tests:
 - a. warning - risk is learned -
 - 1/ shock
 - 2/ increased anxiety
 - 3/ information seeking
 - 4/ realization of profound threat, but not imminent demise
 - 5/ denial and repression are employed
 - 6/ anxiety may increase again by birthdays, diagnosis of other family members, or lapses in cognition/behavior.
 - b. incipient
 - 1/ begins with development of early symptoms of disease - individual is consciously aware that disease is present.
 - 2/ shock, increase fear and anxiety, massive mobilization of psychological defenses.
 - 3/ effect is to isolate and alienate individual from others as well as their own emotional experiences - appears maladaptive but is necessary for further integration and acceptance of diagnosis.
 - 4/ gradually defenses lessen
 - c. breakthrough
 - 1/ presence of disease can no longer be denied.
 - 2/ conscious fear and anxiety - predictive testing.
 - d. diagnosis
 - 1/ even given what the person has been through will have shock and denial, disbelief, disappointment.
 - 2/ relief, no more uncertainty.
 - e. adjustment
 - 1/ challenge of living with a debilitating disease
 - 2/ stages of grief.
- d) Sickle Cell
 1. Woodridge & Murray - noncarriers more negative and benefitted more from counseling than carriers.
- e) Cancer
 1. Lerman, et al. - problem is how to communicate risk and motivate adherence to prevention/detection activities.
 2. Denial and minimization are predominant reactions.
- f) Tay-Sachs -
 1. Female carriers more likely to suffer alone than male.

- 2) Communication 101
 - a) sender
 - 1.
 - 2.
 - 3.
 - b) receiver
 - 1.
 - 2.
 - 3.
- 3) Communication Barriers
 - a) External
 - 1. environment will affect the nature of the session
 - b) Internal
 - 1. Anxiety
 - a. allow to recount past experience
 - b. may have difficulty listening
 - c. may not be logical
 - d. listen for inconsistencies
 - e. observe non-verbal behavior
 - f. high anxiety predicts poor adherence to preventive strategies (Kash, et al; Lerman, et al.)
 - 1/ will specifically need follow-up to assess
 - g. often a mixture of anxiety about what they are to hear and relief at getting accurate information
 - 2. Fear
 - a. "bad news" - won't listen
 - b. fear of spouse disapproval
 - c. may be based on frightening memories
 - 1/ what kind of help can they realistically expect?
 - 2/ formulation of specific plan.
 - d. may need to devote a session to precipitants of fear
 - 3. Anger
 - a. can be either patient or family
 - b. feel life threatened, plans changed
 - c. assume future dependency
 - d. re: pain, fear, anguish, LOSS
 - e. fate unfair
 - f. may die before own children grown or born.
 - 4. Loss of self-esteem
 - a. go from healthy to "sick"
 - b. normal to "carrier"
 - c. situation reveals vulnerabilities
 - d. can create distortion of perception which can lead to misinterpretation of information
 - e. especially prevalent if there was early death of parent
 - f. defective

5. Grief
 - a. for loss of healthy present
 - b. for loss of future
 - c. for anticipated changes in roles
 - d. for body image, sexuality, etc.
6. Denial
 - a. because of fear
 - b. can lead to lack of follow up
 - c. may feel acknowledgement of risk will open door for sadness, depression
 - d. counselor does not know what he/she is talking about
 - 1/ disease isn't as serious as suggested
 - 2/ individual will grow out of problem
 - 3/ tests are misinterpreted
 - 4/ misdiagnosis - not all family members fit pattern
 - e. can be accepting and in denial at different times in same visit.
7. Guilt
 - a. have caused other family members to worry
 - b. have passed on "bad genes"
 - c. "should" have taken better care of family members in the past
 - d. "should" be able to handle with less intense emotion
 - e. other emotions endangered by their "problem" - sad, depressed, loss of sexual pleasure
8. Embarrassment/selfishness
 - a. are taking up too much of the counselors time
 - b. seek repeated care from different professionals
 - c. feel they might be seen as hypochondriacs
 - d. may be a result of physical nature of the problem
 - e. feel problem is insignificant in relation to others
 - f. may feel selfish for getting relatives together for medical records or testing.
9. Insecurity
 - a. especially if parents were ill when client was a child
10. Blame
 - a. in attempt to find cause
 - b. may be barrier for client asking questions
 - c. can be explicit or veiled
11. Chronic sorrow
 - a. parents of affected children
 - 1/ parents feel own imperfections responsible for that of child
 - b. guilt, anxiety, hostility toward whoever made the diagnosis.
12. Stigma
 - a. not as good as others
 - b. either their own feelings or their perception of the feelings of others

- c. may see information as an insult
 - d. may see questions as prying
 - e. may feel private and ashamed especially if defect is visual
 - f. courtesy stigma -
 - 1/ related to someone with genetic disease
 - 2/ personally feel normal but "different" because of relationship with the person
 - 3) certain topics are never entertained in public
 - 4) there may be estrangement from friends.
- 4) Overview of risk disclosure counseling
- a) Pre-test counseling - intake or initial visit
 - 1. Purpose
 - a. to give overview of what will occur
 - b. to establish rapport and prepare for diagnostic visit
 - 1/ both factual and emotional
 - 2/ can allay anxiety
 - c. to provide counselor with awareness of potential impact on family and meaning for them
 - d. provide assessment of speed at which information will be assimilated
 - e. find out what is known about situation for which they are being tested
 - f. give information now - they may not be able to listen later
 - g. determine how they will wait for results - support available to them, etc.
 - b) Post-test counseling - diagnostic visit
 - 1. General - for exams and diagnosis
 - a. Don't rush through information
 - 1/ slow, logical sequence
 - 2/ elicit questions before proceeding
 - 3/ use simple terms - even very intelligent people may have little genetic/medical background
 - 4/ anxiety of the moment may make it difficult to "hear"
 - 5/ watch how many people are present.
 - 2. Positive result
 - a. even when diagnosis is certain, it is rare that there is certain knowledge re: disease status for that person
 - b. make probability and statistics meaningful
 - c. learn main concerns and make it comfortable to ask questions
 - 3. Negative result
 - 4. Indeterminant result
 - a. may cause much anger, may withdraw from counseling
 - b. allow to express disappointment, frustration - there is no more to be learned
 - c) Follow-up
 - 1. Purpose - deal with denial and distortion of information
 - a. negative
 - 1/ may feel disoriented
 - 2/ thought were at high risk

2. make clear not expected to remember everything from other sessions
 3. how did they feel about what they heard
 4. who has been told? If no one, why?
 5. how will information be used?
 6. comment on any unexpected reactions
 7. what did they learn at last visit?
 8. refer if necessary
- 5) Techniques to assess impact
- a) Use of psychological testing
 - b) Assessment of coping skills
 - c) Listen acutely and practice observations skills
 1. Watch and listen for inconsistencies
 2. Inappropriate comments and affect
 3. Non-verbal communication
 4. Sighing
 5. Inaudible words
 6. Incomplete sentences
 7. Tonal quality
 8. Observe family communication process if in group
- 6) When is it appropriate to make referrals?
- a) Sharpe - "a physician who knows, or should know, that the patient's ailment is beyond the physician's professional skills and competence has a duty to refer?"
 1. if doesn't and continues to treat, is held to the same standard of care as that in the speciality
 - b) client must agree there is a distressing problem
 1. ask if there is a wish to alleviate problem
 2. admit you are not expert in solving this type of problem but you know someone who is.
 3. client may feel like a failure, incompetent, or mentally ill.
 - c) counselor must know the therapist to whom the person is being referred
 1. must be comfortable with death, cancer, grief
 2. is ok with uncertainty and appreciates family interactions.

D. Whose feelings are they?

- 1) Proband
- 2) Family
 - a) If family cancer history are more likely to be emotional than those without first hand experience
 - b) May feel urgency to maintain health/strengthen body to overcome perception of increase susceptibility to cancer
 - c) upset because disease is in the family
 - d) fear for affected person
 - e) fear for his/her life
 - f) concern re: own coping ability
 - g) concern about getting the illness

3) YOU

- a) Liaison - reciprocal information sharing for the purpose of best serving the client
 - 1. medical team -
 - a. know who did the telling and what was told
 - b. let medical team know information relevant to their role: e.g., how the person perceived what they were told, what needs to be reinforced, etc.
 - 2. genetic counselor
 - a. inform genetic counselor how individual has been able to perceive information thus far
 - b. your perception of barriers to hearing results of testing
- b) Ongoing support needs
 - 1. for discussion of difficult cases
 - 2. derive benefit of different styles
- c) How do you feel about having only a piece of the information sharing?
How do you feel about discussing genetic cancer susceptibility with people? How do you feel about cancer?

E. Specific counseling issues

- 1) Language
 - a) can intensify emotions
 - 1. deformity
 - 2. deficit
 - 3. abnormality
- 2) Power and influence
 - a) don't become infallible, all-knowing, protector
 - b) empower client and family
 - c) provide information/tools for them to make own decisions
 - d) person/family may want you to give them answers
- 3) Create atmosphere where there is no one right answer
- 4) Be a catalyst
 - a) speed up coping and decision making by helping client work through informational/emotional issues r/t disease
 - b) we are not "bound" to the reaction we facilitate
 - 1. reaffirm confidence in client's ability to problem solve
 - 2. avoid entanglements in disputes
 - 3. maintain objectivity needed to give fresh perspective, but be there for support if needed
 - 4. avoid situation where client is waiting for you to make decision.

- 5) Issues of cultural diversity
 - a) different cultures view health and illness differently
 - 1. Mexican-American - assumed healthy if no overt sign of disease
 - a. may have difficulty accepting diagnosis or understand importance of preventative measures without sign of overt disease
 - b. may believe that disease is sign of God's displeasure
 - b) Decision to seek medical care
 - 1. Italian - seek care when symptoms interfere with relationships
 - 2. Irish - seek care when friends/family agree it should be done
 - 3. Anglo-saxons - seek care when symptoms interfere with activity
 - c) Not always rigid pattern
 - 1. if hear some things which sound irrational to you, investigate if it is a cultural cause
 - 2. know individual's frame of reference
 - 3. spend time learning about what the individual feels is the cause of disease.

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Psychosocial Impact of Cancer Risk Information

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Familial Cancer Risk Counseling Training
May 18, 1995

Post-Session Evaluation

Psychosocial Impact of Cancer Risk Information

| | | | |
|--|------------|-------------|----------------------|
| 1. To what extent did this session meet the stated objectives? | not at all | somewhat | completely met |
| a. the nurse will be able to list 4 common emotional reactions to cancer risk information | | | |
| b. the nurse will be able to discuss how to introduce the need for a mental health referral to the client | | | |
| c. to name an emotional reaction to cancer risk information and describe the counseling response | | | |
| 2. Please rate the teaching effectiveness of the presenter. | not at all | somewhat | completely effective |
| 3. Please rate the relevance of this session to the overall course goal: to provide nurses with the knowledge and skills necessary to provide genetic cancer risk information. | not at all | somewhat | completely relevant |
| 4. Please rate this session for its level of appropriateness for training nurses in Familial Cancer Risk Counseling | too basic | appropriate | too detailed |
| 5. Would you recommend that this session be included in future training programs for Familial Cancer Risk Counseling? | yes | no | |

Please offer any suggestions for future training sessions

Ethical and Legal Implications of Genetic Screening

Objectives

Upon completion of the class, the nurse will be able to:

1. Describe the significance of recent advances in human genetics and the impact within the delivery of health care.
2. Identify the ethical, legal and social issues surrounding the application of genetic technology particularly in the area of diagnostics within cancer care.
3. Discuss the implications of genetic advances on the role of nurses with particular attention to informed consent, truthtelling, confidentiality and discrimination.

Ethical and Legal Implications of Genetic Screening

Presentation

- A. Overview of Genetic Advances - Promises and Pitfalls
 - 1) Genetic Trends
 - a) Predictability of human health
 - b) Knowledge about genetic disorders
 - c) Ability to diagnose disorders presymptomatically
 - d) New genetic tests and screening capabilities
 - e) Potential for gene therapy
 - f) Proliferation of genetic information
 - 2) Identification of inherent ethical, legal and social issues
- B. Impact of Genetic Advances on the Practice of Nurses
 - 1) Review of data collected through grant "managing Genetic Information: Policies for U.S. Nurses"
 - a) Evolving roles related to new genetic technology and information
 - b) Responsibilities of the nurse of genetic screening, testing and counseling
 - c) Practice questions and dilemmas related to burgeoning genetic advances
 - 2) Need for professional guidelines, education and resources to assist nurses in addressing the ethical, legal and professional challenges
- C. Integrating Genetic Testing and Screening into Health Care/Cancer Care
 - 1) Presymptomatic and predictive testing
 - 2) When and how should new tests be introduced into clinical practice?
 - a) What's the goal of testing or screening?
 - b) Are there established criteria?
 - c) Can priorities be set?
 - d) When should testing or screening be recommended?
 - e) How should individuals be informed?
 - f) Will diagnostics be voluntary or mandatory?

- 3) Are all genetic services of equal value? Value/Benefit Determination:
- a) Clinical efficacy
 - b) Optimizing potential
 - c) Reducing morbidity and mortality
 - d) Improving functioning
 - e) Cost effectiveness
 - f) Socially acceptable
 - g) Ethically defensible
 - h) Minimal harms

D. Management of Genetic Information

- 1) What makes genetic information different?
- 2) Issues of acquisition and control
 - a) Who's authorized to collect it?
 - b) How should it be stored?
 - c) How may it be linked to other data?
 - d) Who should control access to it?
 - e) Who should have access to it?

E. Unavoidable Issues/dilemmas in the Care of Patients/Families with Genetic Concerns

- 1) Issues
 - a) Informed consent
 - b) Privacy and confidentiality
 - c) Truthtelling and disclosure
 - d) Discrimination
 - e) Access to services
- 2) Distinctions between decision making in health care and genetics
 - a) Locus of decisional authority
 - b) Models of decision making
 - c) Ethos of non-directiveness
- 3) Professional, ethical and legal obligations of nurses.

F. Visioning Genetics for the Future.

//

**Fox Chase Cancer Center
Familial Cancer Risk Counseling Course for Nurses
May 16-18, 1995**

Colleen Scanlon, RN, MS, JD

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Familial Cancer Risk Counseling Training
May 18, 1995

Post-Session Evaluation

Ethical and Legal Implications of Genetic Screening

| | | | |
|--|------------|-------------|----------------------|
| 1. To what extent did this session meet the stated objectives? | not at all | somewhat | completely met |
| a. to describe the significance of recent advances in human genetics and the impact within the delivery of health care | | | |
| b. to identify the ethical, legal and social issues surrounding the application of genetic terminology particularly in the area of diagnostics within cancer care | | | |
| c. to discuss the implications of genetic advances on the role of nurses with particular attention to informed consent, truth-telling, confidentiality and discrimination | | | |
| 2. Please rate the teaching effectiveness of the presenter. | not at all | somewhat | completely effective |
| 3. Please rate the relevance of this session to the overall course goal: to provide nurses with the knowledge and skills necessary to provide genetic cancer risk information. | not at all | somewhat | completely relevant |
| 4. Please rate this session for its level of appropriateness for training nurses in Familial Cancer Risk Counseling | too basic | appropriate | too detailed |
| 5. Would you recommend that this session be included in future training programs for Familial Cancer Risk Counseling? | yes | no | |

Please offer any suggestions for future training sessions

PANEL DISCUSSION
Administrative Issues in Establishing Cancer Risk Assessment Services
Brief Outline

- I. Family Risk Assessment Program (FRAP) Description
 - A. Target Population
 - B. Group Education Session
 - C. Ongoing Clinic
 - D. Database

- II. Recruitment
 - A. Marketing
 - B. Obtaining Baseline Information

- III. Scheduling
 - A. Group Education Session
 - B. Clinic Appointments
 - C. Long Term Follow-up

- IV. Correspondence
 - A. Letters of Recommendations
 - 1. Participants
 - 2. Identified Physicians
 - B. Pedigrees
 - C. Follow-up Appointment Reminder Letters

- V. Questionnaires
 - A. Baseline Survey Packet
 - B. Annual Follow-up Surveys

- VI. Billing Procedures

Panel Outline

Issues and Implications for Establishing Cancer Risk Assessment Services

I. Physician Barriers

1. Awareness-Knowledge Base
2. Time Constraints
3. Financial Barriers (Era of Managed Care)
4. Uncertainty regarding implications of testing and risk notification
5. Uncertainties regarding screening, chemoprevention, surgical prevention options and/or true benefit of these interventions.

II. Potential Interventions

1. Educational interventions aimed at primary care physicians (family practice, primary care, OB/GYN...).
2. Commitment from insurance carriers and managed care providers to provision of these services.
3. Establish guidelines or clinical pathways regarding management of patients in this setting.
4. Identify referral sources as well as sources of support.

II. Risk Assessment in Underserved Populations - Special Challenges

1. The inclusion of minority populations in cancer risk assessment research and service is critical.
2. Requirements for inclusion of minorities
 - basic understanding of social structure
 - communication and language style are critical
 - attitudes towards disease must be understood
 - patterns of authority within each community must be understood
 - other barriers must be identified
3. The presentation of information in a linguistically and culturally appropriate manner can be accomplished.
4. Issues such as the importance of religion, the importance of the family unit, the male figure/sexuality, as well as the particular populations outlook on research and their emphasis on privacy must all be evaluated once dealing with this type of effort.
5. Preliminary focus group findings will be presented regarding the provision of cancer risk counseling to underserved populations.

PANEL OUTLINE

Implications for Establishing Cancer Risk Assessment Services

- I. Nursing practice Models - how current programs can serve as models for adaptation for Cancer Risk Assessment.
 - A. Comprehensive Breast Care Program
 - 1. Program implementation - issues in establishing a new program
 - 2. Services offered
 - 3. Future trends

APPENDIX

**Listing of Regional Cancer
Risk Screening Programs**

Cooper Hospital /University Medical Center
Cancer Risk Counseling Program
3 Cooper Plaza Suite 220
Camden, NJ 08103
(609) 963-3572

Fox Chase Cancer Center
Family Risk Assessment Program
510 Township Line Road
Cheltenham, PA 19012
(215) 728-2792

Johns Hopkins Hospital
600 N. Wolfe Street
Baltimore, MD 21205
(410) 639-5200

Lombardi Cancer Center
Cancer Prevention / Control Department
Georgetown University Hospital
2233 Wisconsin Avenue
Washington, DC 20007

Memorial Sloane Kettering
Breast Center
205 E. 64th Street
New York, NY
(212) 794-4900

Monmouth Medical Center
300 Second Avenue
Long Branch, NJ 07740
(908) 870-5360

Strang Cancer Prevention Center
428 E. 72nd Street
New York, NY 10021
(212) 794-4900

University of Pennsylvania Cancer Center
3400 Spruce Street
6 Penn Tower
Philadelphia, PA 19104-4283
(215) 349-8141

**Listing of ONS Members
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ISONG**

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Attendee: _____

POST TEST QUESTIONS

Principles of Basic Genetics

1. Match each genetic disorder on the left with the correct inheritance pattern.
(Autosomal Dominant = **AD**; Autosomal Recessive = **AR**; X-linked = **X**;
Chromosomal = **C**; Multifactorial, polygenic, non-Mendelian = **M**).

- | | |
|-----------------------------------|-------|
| a) Cystic Fibrosis | _____ |
| b) Huntington's Disease | _____ |
| c) Fragile X | _____ |
| d) Arthritis | _____ |
| e) Phenylketonuria | _____ |
| f) Down's Syndrome | _____ |
| g) Neurofibromatosis, type I | _____ |
| h) Non-insulin dependent diabetes | _____ |
| i) Turner Syndrome | _____ |
| j) Tay Sachs Disease | _____ |
| k) Marfan Syndrome | _____ |
| l) Cancer (tricky!) | _____ |

2. Human chromosomes are composed of a complex of all except which one?
- a) DNA
 - b) histones (basic protein)
 - c) non-histone protein
 - d) RNA

[ANSWER: ____]

Molecular genetics of carcinogenesis

3. Which of the following is not a stage of carcinogenesis?
- a) initiation
 - b) mutation
 - c) promotion
 - d) progression.
4. Which best describes a type of genetic change associated with cancer?
- a) autosomal transmission
 - b) phenotypic expression
 - c) mismatch repair genes.

[ANSWER: ____]

[ANSWER: ____]

5. A gene that induces uncontrolled cell growth and proliferation is which of the following?

- a) oncogene
- b) tumor suppressor gene
- c) candidate gene.

[ANSWER: ____]

Human Genome Project and Genetic Testing

6. The primary goals of the human genome project include:

- a) Constructing detailed genetic linkage maps
- b) Isolating the genes contained within chromosomes
- c) Constructing physical maps of chromosomes.
 - 1) a and b
 - 2) b and c
 - 3) a, b, and c.

[ANSWER: ____]

7. Which of the following is not a method of direct testing?

- a) DNA sequencing
- b) Linkage analysis
- c) PCR.

[ANSWER: ____]

8. Which of the following techniques can amplify a DNA sequence, hundreds of millions of times in a matter of hours?

- a) FISH
- b) Cloning
- c) PCR.

[ANSWER: ____]

Inherited Patterns of Cancer

9. What are some of the indications obtained from a family history that would necessitate further cancer genetics counseling and screening?

- a) Breast, ovarian and/or other clusters of cancer;
- b) Bilateral breast cancer;
- c) Early age of onset (before age 45);
- d) Multiple primary tumors;
- e) Vertical transmission of cancers and in multiple family members;
- f) All of the above.

[ANSWER: ____]

10. Which organ is not considered as part of the spectrum of organs at risk for tumors in the Hereditary Non Polyposis Colorectal Cancer Family Syndrome (HNPCC)?

- a) colon;
- b) ovary;
- c) endometrium;
- d) stomach;
- e) brain.

[ANSWER: ____]

11. Which cancer genetic syndrome is not considered as part of the Polyposis and Non-Polyposis Colorectal Cancer Family Syndromes?

- a) Familial Adenomatous Polyposis (FAP);
- b) Flat Adenoma Syndrome (FAS);
- c) Lynch I (HNPCC I);
- d) Peutz-Jegher Syndrome;
- e) Li-Fraumeni Cancer Family Syndrome.

[ANSWER: ____]

Obtaining and interpreting family history information

12. Which of the following would not be included as a purpose for obtaining a cancer family history?

- a) To formulate cancer risk diagnosis
- b) To educate client
- c) To change a client's perception of risk
- d) To provide basis for cancer screening guidelines.

[ANSWER: ____]

13. Ideally, data on how many generations should be included in the family history?

- a) one
- b) two
- c) three.

[ANSWER: ____]

14. What steps would you take to confirm a cancer diagnosis in a maternal aunt of the proband?

- a) Verbally confirm diagnosis with the aunt
- b) confirm diagnosis from medical records
- c) b only
- d) a & b.

[ANSWER: ____]

15. What information would you obtain on family members who have had cancer?
- a) Cancer site
 - b) Number of primary cancers
 - c) Age at diagnosis
 - d) Environmental exposures
 - e) All of the above.

[ANSWER: ____]

Familial Cancer Risk Information

16. A risk estimate that provides an estimation of cancer risk for each subsequent decade of life based on specific variables is called:

- a) relative risk
- b) lifetime risk
- c) cumulative risk
- d) absolute risk.

[ANSWER: ____]

17. The Claus model allows for estimation of risk for individuals with a family history of which cancer:

- a) breast
- b) ovarian
- c) colon.

[ANSWER: ____]

18. BRCA1 carriers are estimated to have a lifetime risk for breast cancer that may be as high as:

- a) 50%
- b) 75%
- c) 90%.

[ANSWER: ____]

19. Which risk model would provide the most appropriate estimate of risk for a woman undergoing regular screening for breast cancer and having a sporadic family pattern of breast cancer:

- a) Claus model
- b) Gail model
- c) LOD score.

[ANSWER: ____]

Nursing Role in Providing Familial Cancer Risk Information

20. Which are the best models for providing risk information for an individual with familial pattern (moderate risk) for breast cancer?

- a) relative risks
- b) cumulative
- c) family history.
 - 1) a only
 - 2) c only
 - 3) a and b
 - 4) b and c.

[ANSWER: ____]

21. Which of the following is critical to complete before providing an individual or family with risk information and medical follow-up recommendations?

- a) Obtain a cancer family history only
- b) Correct an individual's misperception of risk
- c) Obtain a cancer family history and have cancer diagnoses confirmed.

[ANSWER: ____]

22. Which of the following reasons might explain why someone with a strong family history of cancer may not have a hereditary cancer?

- a) Shared environment
- b) A common cancer in large family pedigrees may occur more often by chance
- c) a and b.

[ANSWER: ____]

Medical Management and Surveillance

23. Prophylactic surgery provides 100% efficacy in preventing a cancer.

- a) True
- b) False

[ANSWER: ____]

24. Which of the following are potential risks associated with prophylactic surgery?

- a) Psychological risk
- b) Surgical complications
- c) Need for hormone replacement.
 - 1) a & b
 - 2) b & c
 - 3) all of the above.

[ANSWER: ____]

25. Which of the following experimental methods are most utilized in screening for ovarian cancer in high risk women?

- a) Pelvic exam, CEA & transvaginal ultrasound
- b) CT scanning and pelvic exam
- c) Pelvic exam, CA125, and transvaginal ultrasound.

[ANSWER: ____]

Psychosocial impact of cancer risk information

26. True or False:

Emotional reactions to cancer risk information include anxiety, fear, embarrassment and guilt.

- a) True
- b) False.

[ANSWER: ____]

27. You have recognized that the client is in need of a referral to a mental health professional. You tell the client which of the following?

- a) Many people get depressed and need medication after being told of genetic risk for cancer.
- b) You ask the client if they believe there is a problem which they would like to address.
- c) You are not the right person to help the client address his/her problem.
- d) You know the counselor to whom you will refer the client.
- e) You must refer to a counselor because of legal issues.

[ANSWER: ____]

28. A woman comes to your clinic and learns that she is at increased risk of breast cancer. Her mother died five years ago of the same disease. As the client tells you how guilty she feels at not spending more time with her mother during her last months, you respond by:

- a) Telling her that guilt is a wasted emotion and that she will need all of her emotional energy channeled toward fighting her own disease.
- b) Allowing her time to discuss what she did do to care for her mother, encouraging her to see that she did what her time/energy permitted her to do during a frightening, difficult time.
- c) Telling her to relate the story to her daughter so that her daughter does not have the same regrets later.

[ANSWER: ____]

Visioning Genetics for the Future

29. Which of the following are considered ethical and/or legal concerns related to predictive testing for cancer susceptibility?

- a) Informed consent
- b) Privacy and confidentiality
- c) Discrimination issues
- d) All of the above.

[ANSWER: ____]

30. Which of the following criteria is not used to determine the appropriateness of introducing new genetic diagnostics into clinical practice?

- a) Clinical efficacy
- b) Cost-effectiveness
- c) Limited number of family members
- d) Reduction in morbidity and mortality.

[ANSWER: ____]

Familial Cancer Risk Counseling Training
May 16,17, and 18,1995

Program Evaluation

| | | | |
|---|------------|----------|----------------|
| 1. To what extent did this program meet the overall course goal to provide nurses with the knowledge and skills necessary to provide genetic cancer risk information? | not at all | somewhat | completely met |
| | | | |
| 2. How useful was the program in providing you with skills that can be used in oncology nursing practice? | not at all | somewhat | very useful |
| 3. How effective were the following aspects of the program in meeting the course objectives? | not at all | somewhat | very effective |
| a. the homework task of drawing your own pedigree | | | |
| b. the role modeling of taking a family history | | | |
| c. taking a family history by the group | | | |
| d. the role modeling of giving risk information | | | |
| e. the role playing sessions in taking a family history and giving risk information | | | |
| f. the panel discussion | | | |

Comments:

What I liked best about the course _____

I would have like more information about _____

Changes or suggestions I would make for future programs _____

Thank You

APPENDIX F

FAMILIAL CANCER RISK COUNSELING: DEVELOPMENT AND EVALUATION OF A
TRAINING PROGRAM FOR NURSES. Agnes Masny, RN, MPH, and Fredrica Preston,
MA, AOCN, CRNP, Fox Chase Cancer Center, Philadelphia, PA 19111

Oncology practice is being revolutionized by the availability of molecular genetic tools to assess cancer risk. Since most nurses have received little or no formal training in cancer genetics, this area of oncology presents challenging opportunities for nursing education and practice. The purpose of this project was to develop a curriculum, and to test the impact of training nurses in Familial Cancer Risk Counseling (FCRC). The project had two phases: 1) development and implementation, and 2) evaluation. Formative and outcome evaluations were used in each phase respectively. During the development phase, 14 key informant interviews were conducted with nurses working in cancer risk assessment; and four focus groups were held with 29 community-based nurses. Findings from this phase identified key concepts for the curriculum including principles of basic genetics, molecular genetics of carcinogenesis, inherited patterns of cancer, obtaining and interpreting a cancer family history, and the role of nursing in FCRC. The focus groups indicated that practicing skills for family history taking, pedigree development, and communicating risk were essential. Additional issues identified were medical management of high risk individuals, the psychological impact of cancer risk information, the legal and ethical implications, and administrative issues in establishing cancer risk assessment services. Based on this information, a curriculum was developed and a three-day training was conducted with 36 oncology nurses. Of these, 61% were masters prepared, 16% currently worked in risk assessment, 33% planned to initiate cancer risk programs, and only 8% had taken a formal course in genetics. To evaluate the course objectives, pre/posttest measures of knowledge and a subjective evaluation of course objectives were used. There was a statistically significant improvement in pre and posttest knowledge scores ($p = .0001$) using the Wilcoxon signed rank statistic, with a mean pretest score of 58% and mean posttest score of 76%. The course objectives were rated "completely met" by 80% of participants. To test the impact of the course, survey data at baseline and at 6 month post-training will analyze individual and group change over time in the nursing role and confidence in providing FCRC. At baseline, 56% were routinely taking a cancer family history. Of these, 50% obtained information on first degree relatives only, 35% failed to record age at diagnosis, and 60% failed to inquire about bilaterality of disease. Only 5% felt "very confident" in their role. Research articles were cited as the primary source of information in cancer genetics (51%); and 64% listed continuing education as the greatest need to providing FCRC. This study provides information on core concepts for training oncology nurses in cancer genetics and suggests that education in familial cancer risk counseling is an essential step towards integrating principles of cancer genetics into oncology nursing practice.

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- Research Issue

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same data set?☐ Yes ☐ No

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Name & Credentials Agnes Masny, RN, BS, MPHPreferred Mailing Address 510 Township Line RoadCheltenham, PA 19012Telephone (work) (215) 728-2892 (home) (215) 886-8647

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Where _____

Where _____

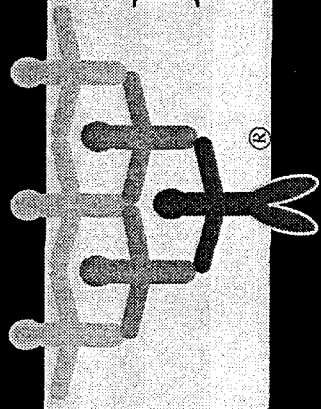
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Signature of primary author _____

APPENDIX G

Breast Flip Chart/Slide Table of Contents

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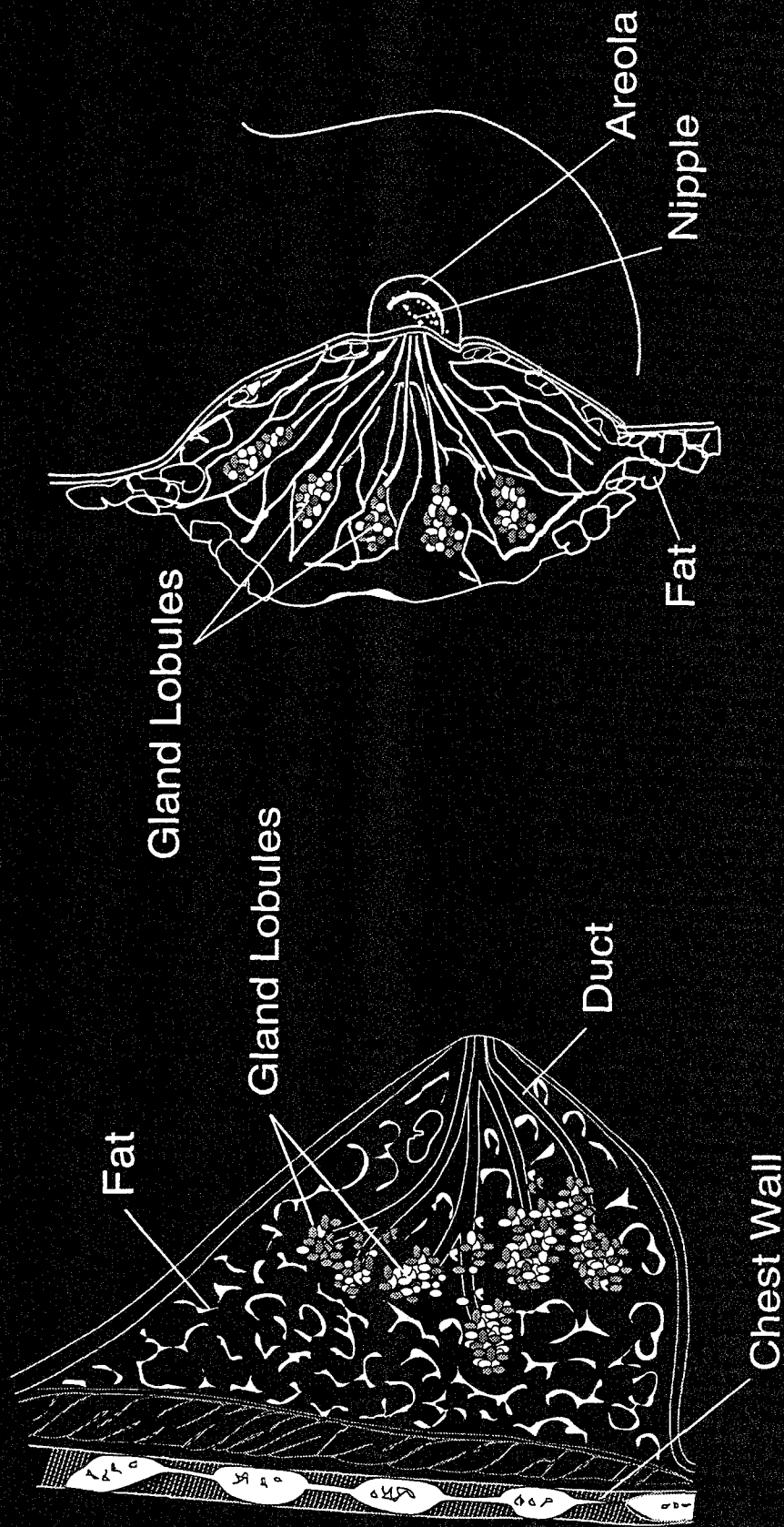
Breast Cancer Family Program

- Normal anatomy & development
- Risk factors
- Genetics
- Personal risk
- Early detection

Breast Cancer Family Program

- Welcome
- Five key topics to cover
 - Normal anatomy & development of the breast
 - Risk factors associated with breast cancer
 - The genetic changes related to breast cancer, particularly in certain families where there are several cases of cancer.
 - We are going to give you an estimate of your personal risk for breast cancer
 - Prevention and early detection

Breast Anatomy

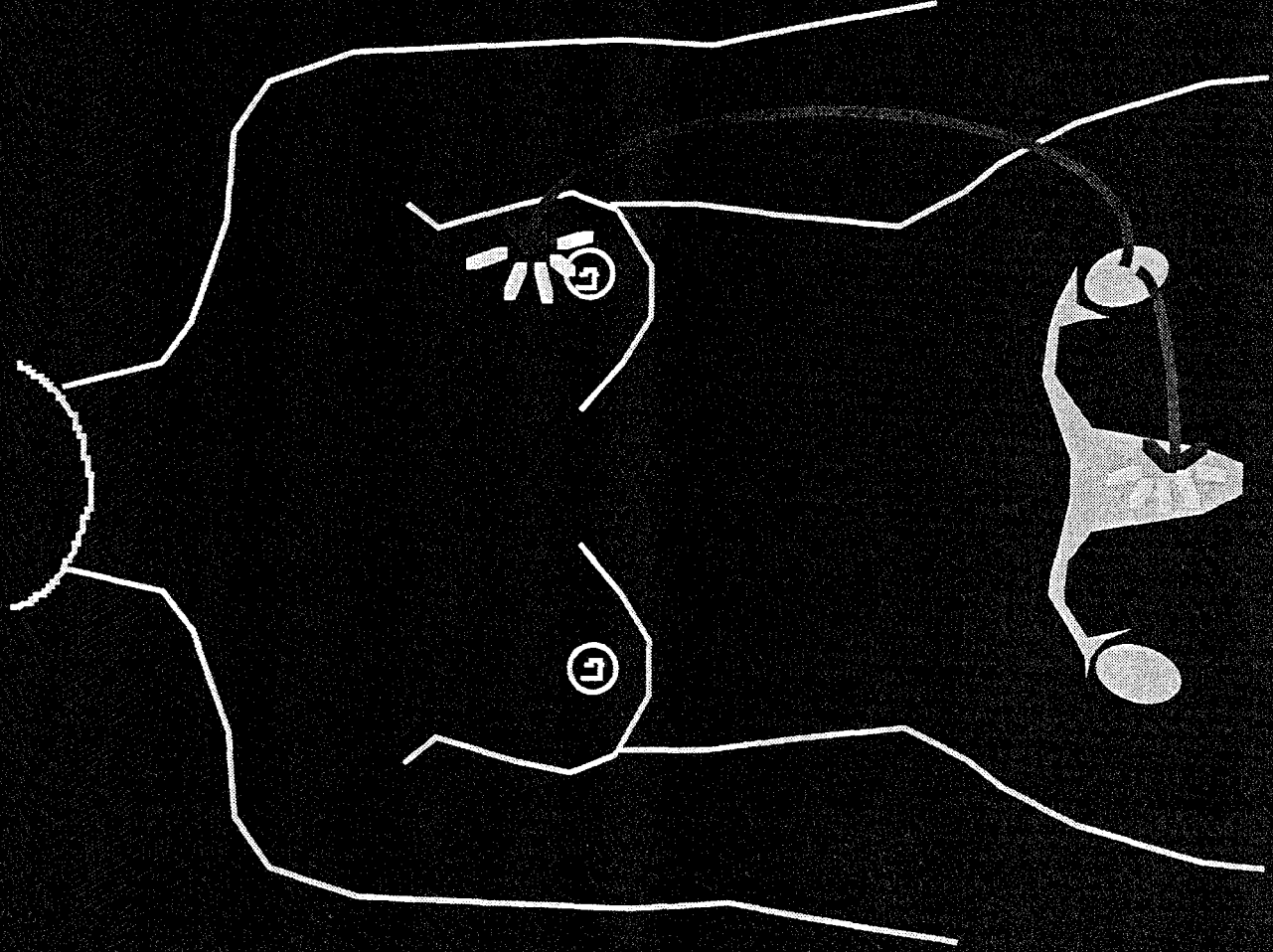


Breast Anatomy

- Normal mature breast contains thousands of tiny sac-like glands
- Designed to secrete milk during lactation
- The glands empty into ducts (or tubules) which form a series of larger and larger ducts that finally lead to the nipple.
- The rest of the breast consists of fat and connective tissue that protects the glands.
- Most women can feel these glands when doing a breast exam.
- Breast cancer occurs in the glands or ducts.

ESTROGEN

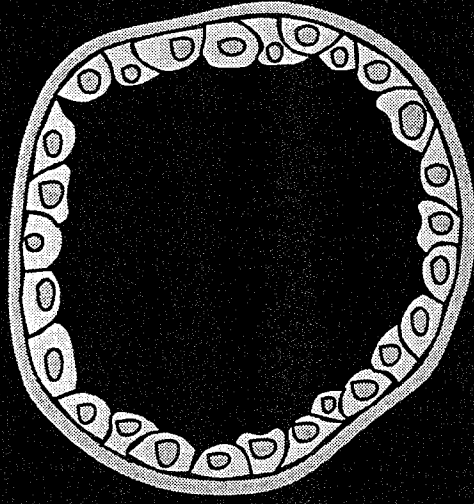
Estrogen from the
ovaries stimulates
changes in the uterus
lining and the breasts



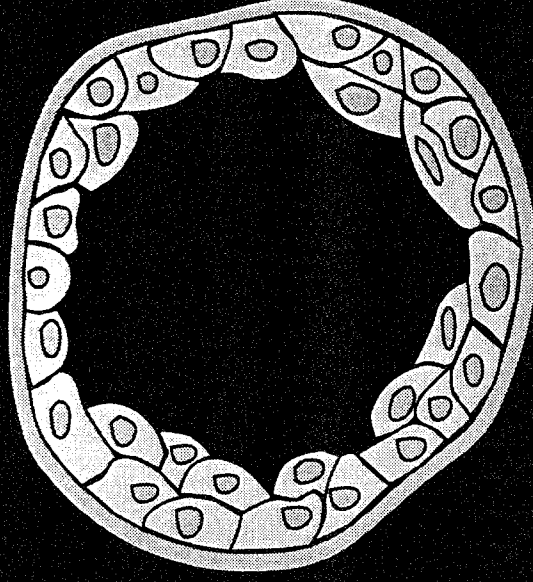
Estrogen

- Secreted by the ovaries
- Stimulates changes in the breast glands and ducts and the lining of the uterus (menstruation)
- Estrogen peaks in the blood just before menstruation
- This is why a woman's breast will be larger, tender, and possibly feel lumpier just before her period.

Breast Function



After Menstruation



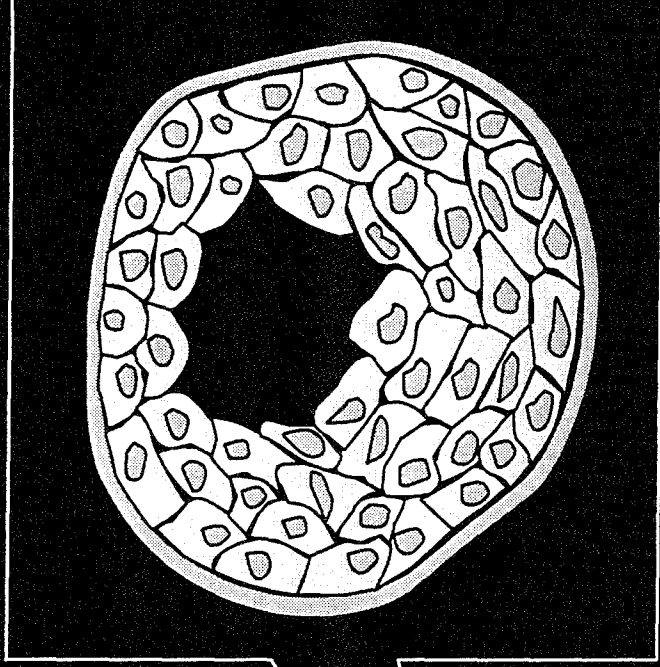
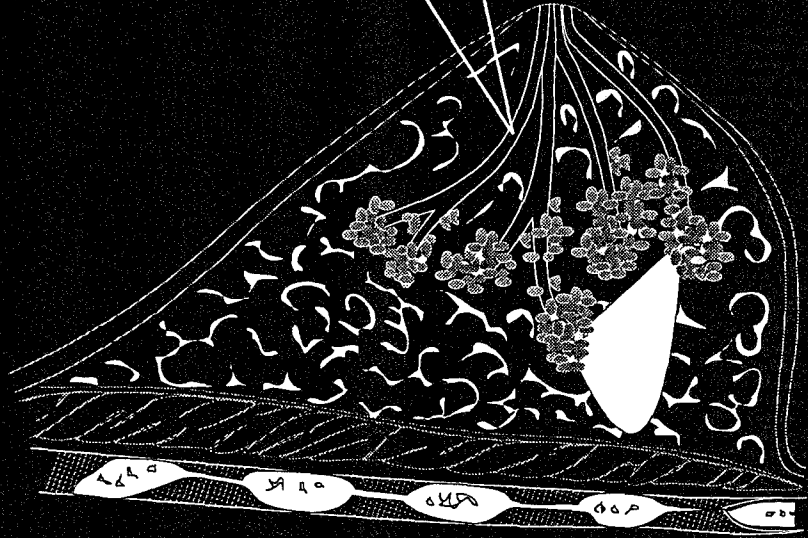
Before Menstruation

Inside the Ducts

Breast Function

- Estrogen causes the cells lining the ducts and glands to swell **and** increase in number.
- Anytime there are new cells produced, it means genetic material is being passed on to these new cells.
- Whenever genetic material is passed on, there is a potential for a mistake or mutation to occur.
- The breasts are unique organs because the cells are being affected this way on a monthly basis. These frequent changes means the breasts have a higher risk of mutations than other, more stable organs. The ovaries are another example of an organ that is constantly changing. So is the skin, which is why skin cancer is so common.

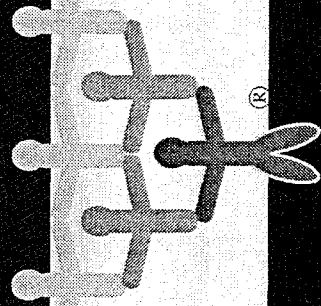
Ductal Carcinoma In Situ (DCIS)



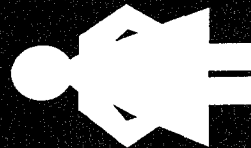
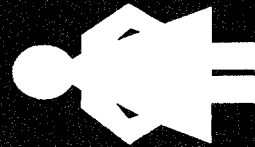
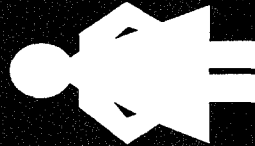
Many abnormal cells
within the duct

Ductal Carcinoma In Situ Picture

- Very Early Stage Cancer
- Can see the changes in the cells under a microscope
- But would not be felt



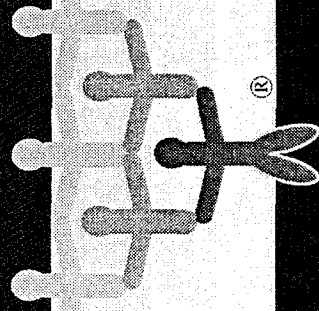
RISK



**Breast cancer affects 1 in 9 women in the U.S.
(risk from birth to age 85)**

Risk

- The possibility that any individual woman will develop breast cancer in her lifetime is sometimes called risk.
- Breast cancer affects about 1 in 9 women in the United States.
- The risk figure is based on a woman living until age 85.
- Risk varies from woman to woman, and some women are more likely to get breast cancer than others.
- The things that increase a woman's risk are called risk factors.
- This 1 in 9 figure does not give a clear picture of risk because it takes into account women who have multiple risk factors and women who have very few risk factors.



Risk Factors

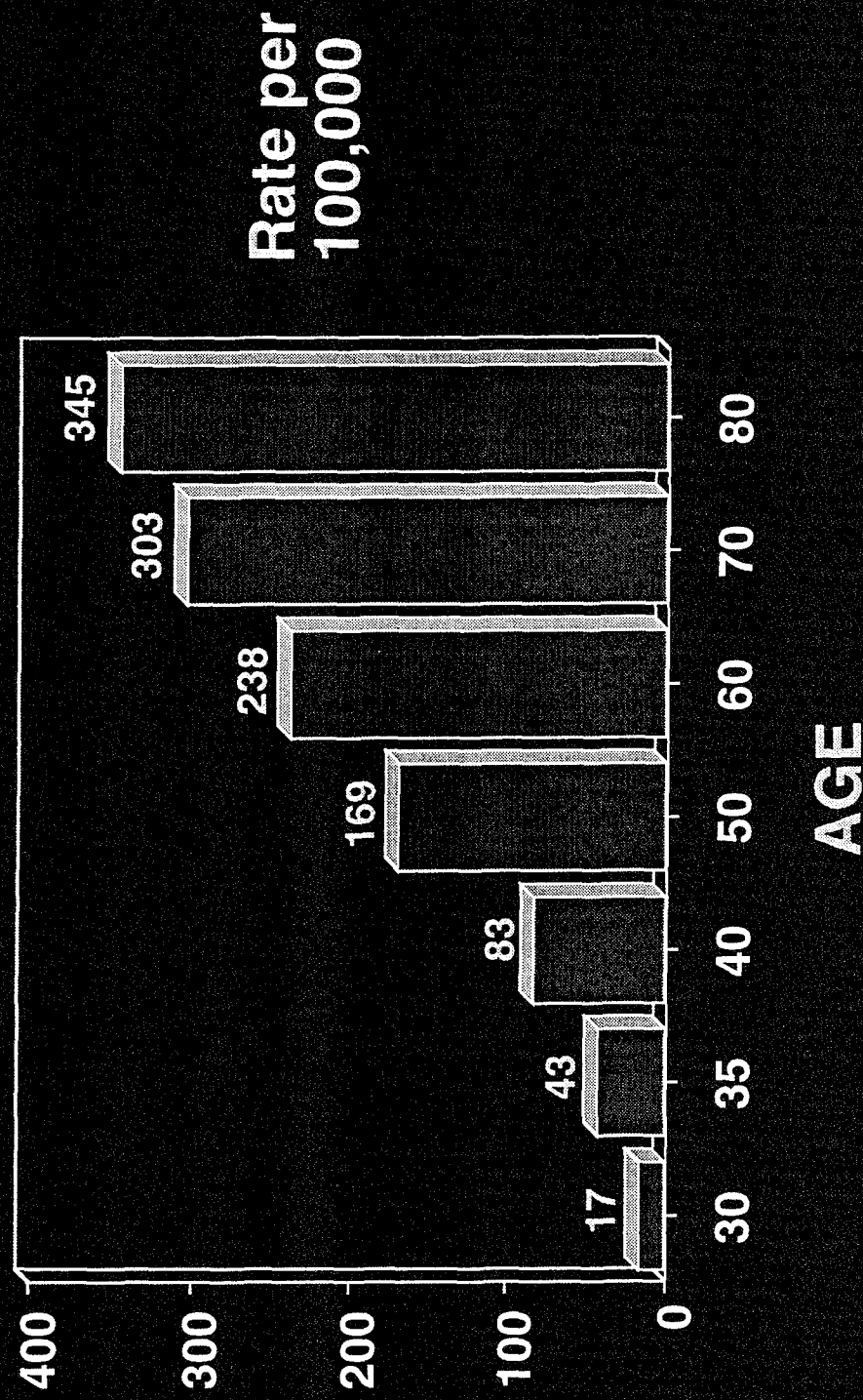
- **Age**
- **Family history**
- **Menstrual history**
- **Childbearing history**
- **Breast biopsy history**
- **Personal history of breast cancer**

Risk Factors

- Age
- Family History
- Menstrual History
- Childbearing History
- Breast Biopsy History
- Personal History of Breast Cancer

[These are listed on individual's data sheet. Factors that increased individual's risk percentage have been checked.]

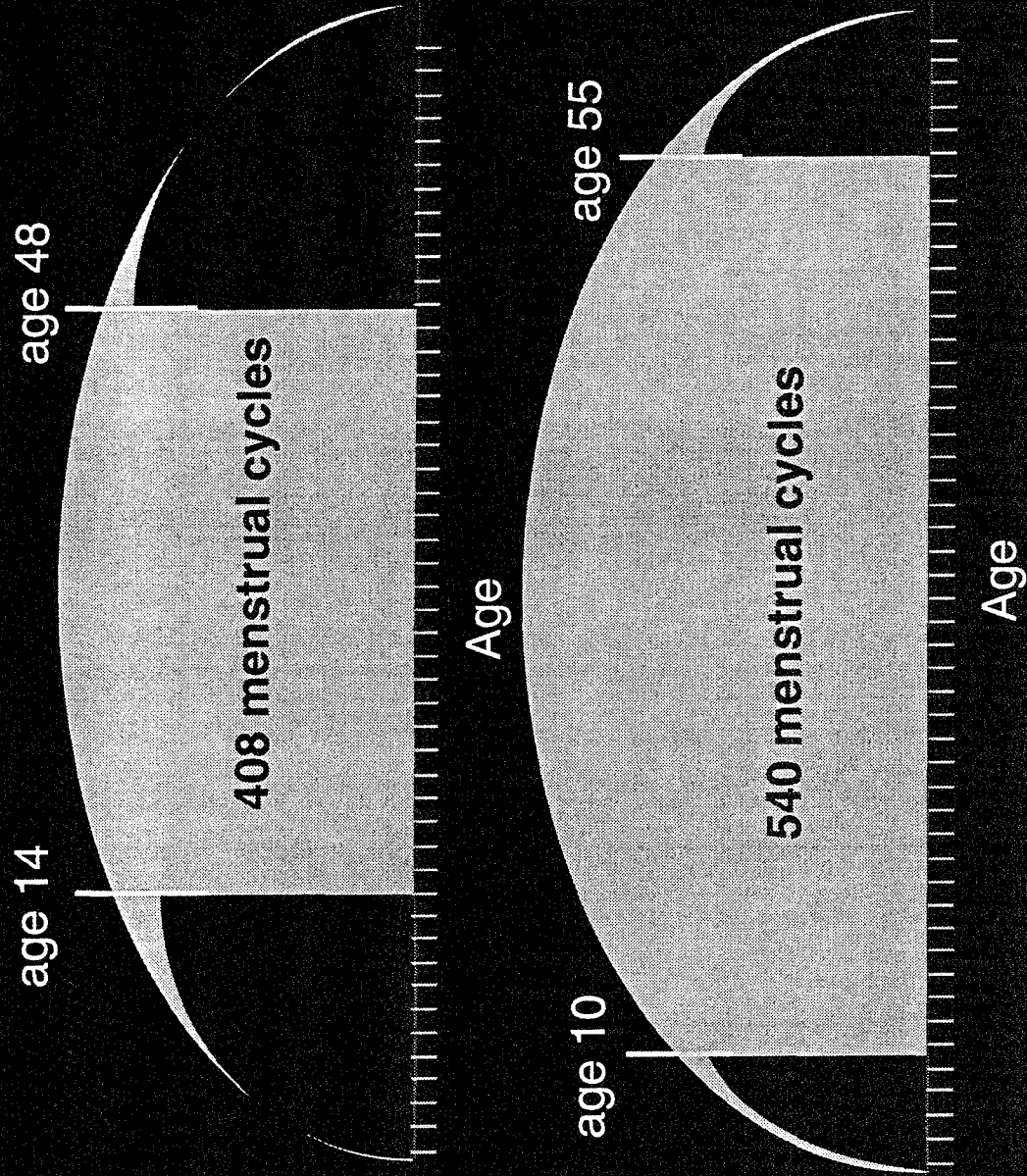
Average risk of developing breast cancer in a given year in white women.



Age

- In general, age is the most important risk factor.
- As you get older, your chances of getting breast cancer increase.
- This graph shows that the risk of getting breast cancer increases each decade of life.
- Two thirds of the cases of breast cancer occur in women over age 50.
- In women with a strong family history of breast cancer, breast cancer can occur at an earlier age, sometimes even in 20s and 30s. We'll talk more about that in a few minutes.

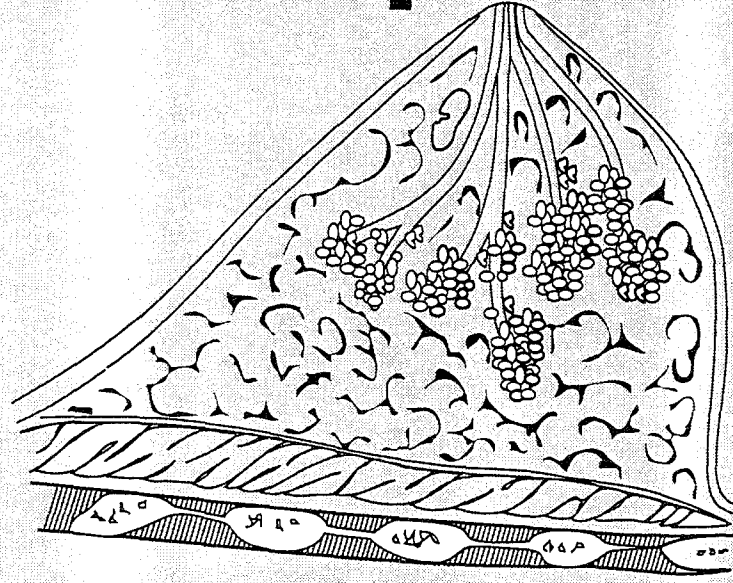
Menstrual History



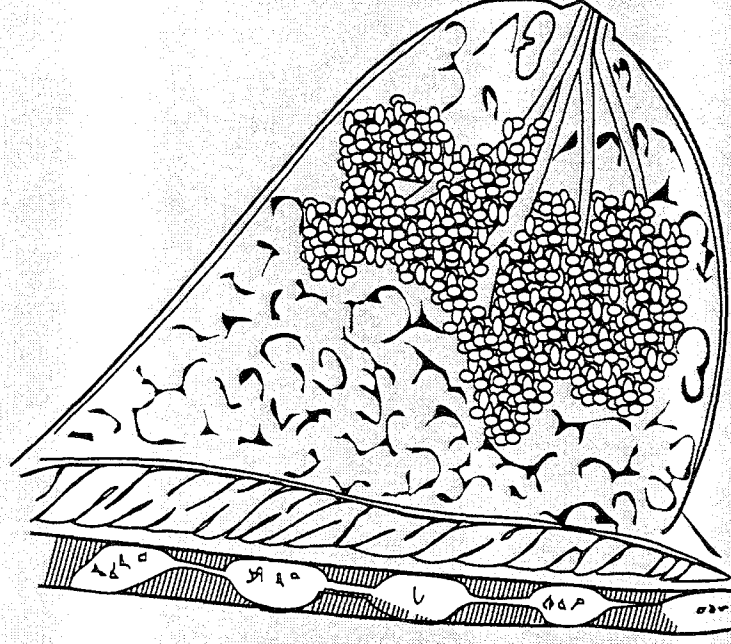
Menstrual History

- If a woman was very young, age 9, 10, or 11, when she had her first menstrual period, her risk is slightly increased.
- If she was 12 or 13, her risk would be slightly increased but not as much as if the period began younger than this.
- If she was 14 or older, it does not affect risk.
- The older a woman was at menopause, the greater her chances of developing breast cancer.
- The more years that ovaries are active and producing estrogen -- that is the more years a woman has her periods -- the more chance it will affect her breast tissue in a way that makes her more susceptible to breast cancer.

Breast tissue changes during pregnancy and lactation:



mature breast



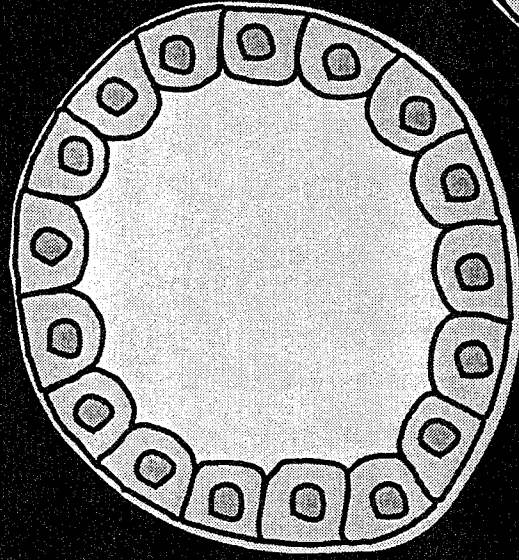
during pregnancy & lactation

Further breast tissue development

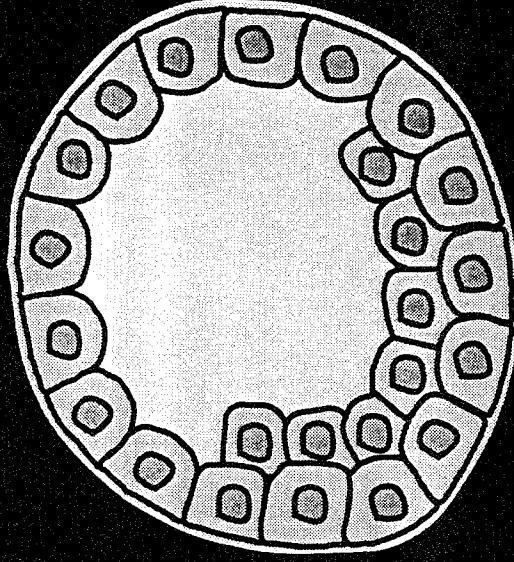
Breast Tissue Changes During Pregnancy

- This diagram shows a breast with the glands, ducts, and lobules in a mature state.
- It also shows a breast during pregnancy and lactation which increases the number and size of the lobules.
- It is thought that this change in breast tissue during pregnancy and lactation helps to further mature the breast which will make it more stable and less vulnerable to change.
- This is thought to have a preventive effect.
- Childbearing -- In general, a woman's risk for breast cancer tends to increase as the age at first birth increases.
 - Women who have never given birth also tend to have a higher risk of breast cancer.
 - This does not appear to be the case in women who have a family history of breast cancer.
 - The risk associated with having an FDR with breast cancer appears to override the effect of a woman's age at first live birth, or whether she has never given birth.
 - The reasons for this are not clear.

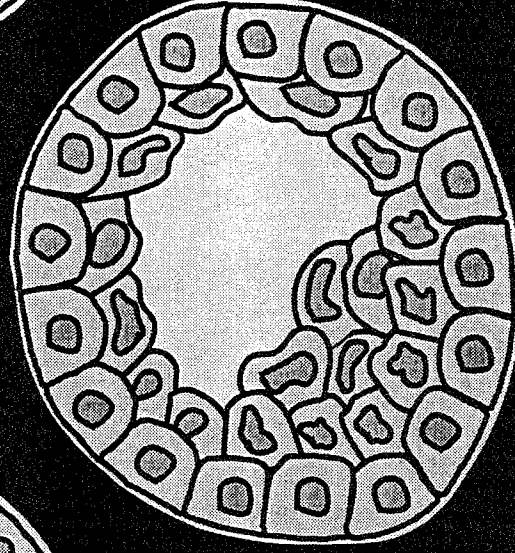
Changes within the duct



Normal duct



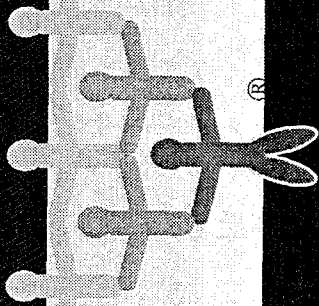
Hyperplasia



Atypical hyperplasia

Breast Biopsy--Changes within the Duct

- Breast biopsy results can sometimes give us information about a woman's risk for breast cancer.
- There is normally a single layer of cells lining the duct.
- Hyperplasia means that there are additional cells lining the ducts.
- Atypical Hyperplasia: There are more cells lining the duct, and these cells have changed and have become irregular.
- It is not the breast biopsy itself that increases breast cancer risk, but certain conditions that can be diagnosed by a biopsy, such as atypical hyperplasia, that may increase risk.

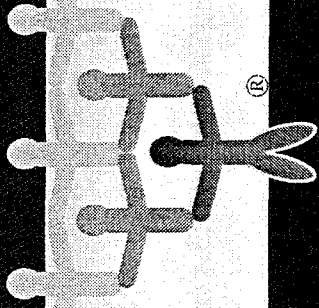


Breast Biopsies & Risk

| Diagnosis | Risk |
|--|------------------|
| Benign | no change |
| Hyperplasia without atypia no family history with family history | mild mild |
| Atypical Hyperplasia no family history family history | moderate high |

Breast Biopsies and Risk

- Benign
 - Most lumps that are biopsied are diagnosed as benign and do not increase a woman's risk for breast cancer.
 - A small percentage of benign lumps are classified as gross (large) cysts, which carry a slightly higher breast cancer risk.
 - This risk will increase moderately if the woman has a gross cyst and an FDR with breast cancer.
- Hyperplasia Without Atypia
 - Some changes in the cell, but no features of cancer.
 - Women with hyperplasia have a mildly elevated risk for breast cancer.
 - This risk is slightly higher if she also has a FDR with breast cancer.
- Atypical Hyperplasia
 - Cells have some, but not all, of the features of cancer.
 - Only 4% of biopsies fall into this category.
 - Does increase breast cancer risk, especially if there is a family history of breast cancer.



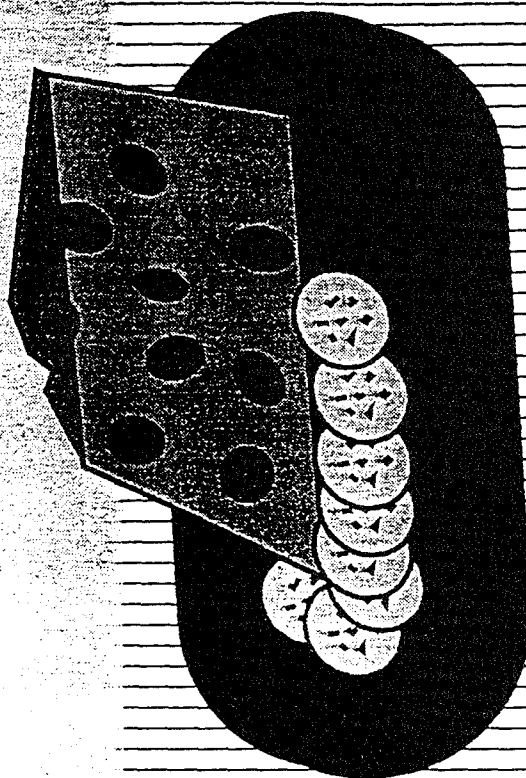
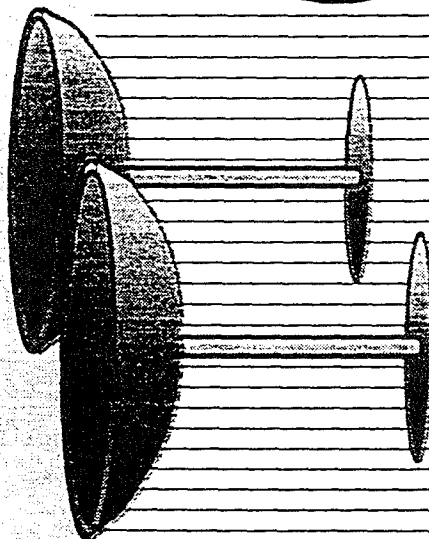
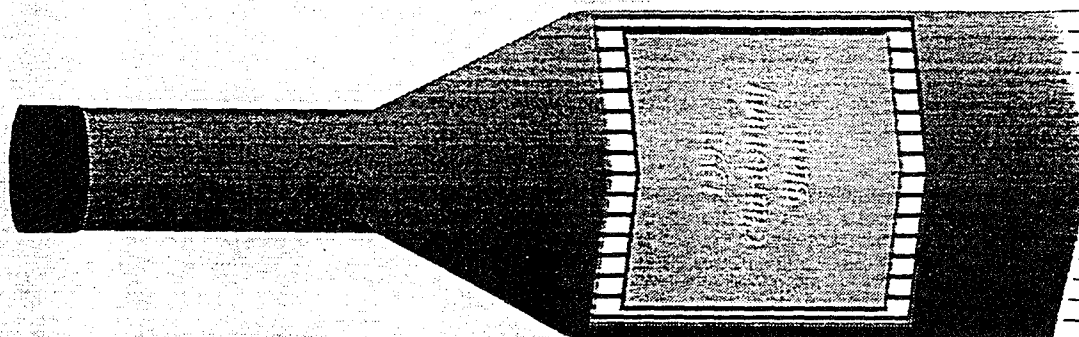
Other Factors?

- Diet
- Vitamins & minerals
- Weight
- Hormones
- Exercise

Other Factors

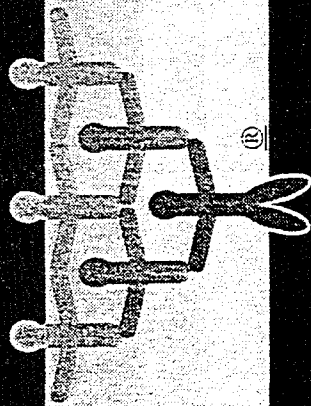
- There are several other factors which can influence a woman's risk for breast cancer.
- We have good information on some factors, such as alcohol; but on others, such as diet and exercise, the evidence is less conclusive
- We will discuss each of these factors now

Diet & Alcohol

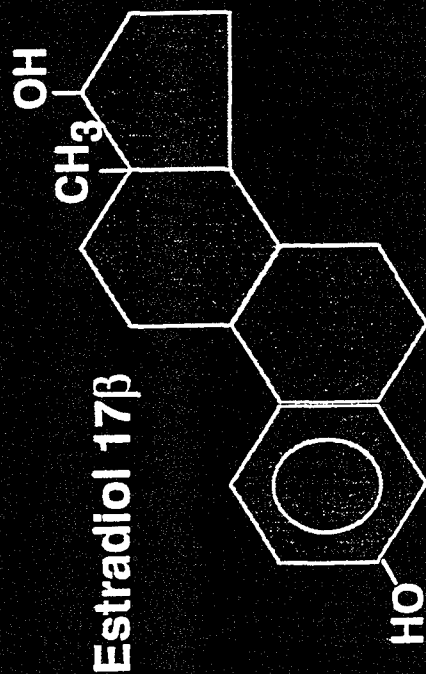
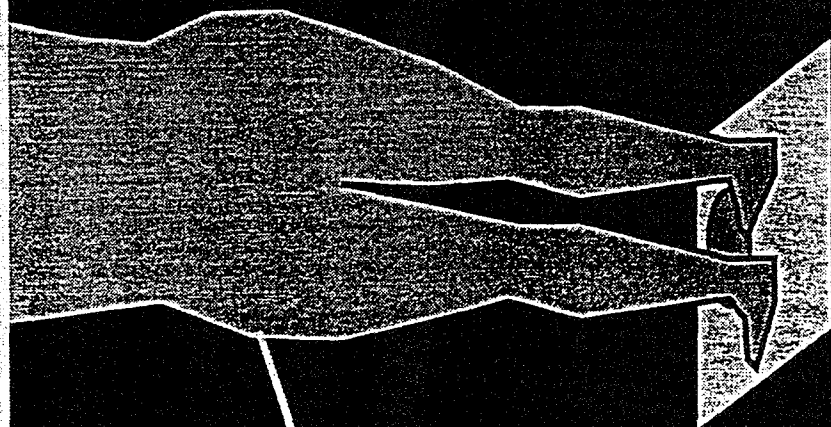


Diet & Alcohol

- Diet
 - Several studies have looked for a relationship between diet and breast cancer.
 - Dietary fat is the nutrient that has been most strongly suspected.
 - Studies comparing breast cancer rates in several countries found that countries with the highest intake of fat also have the highest rates of breast cancer.
 - Not all studies support this.
 - A study currently being conducted will follow women over several years to see if a low fat diet reduces their breast cancer risk. We are several years away from the results.
- Vitamins and minerals
 - Vitamin A and beta carotene (the vegetable form of Vitamin A) and the mineral selenium have been found to reduce the rates of certain cancers in laboratory rats.
 - Not sure how this translates to humans; but research continues.
- Alcohol
 - Alcohol use is associated with breast cancer risk.
 - Particularly for women who started drinking at a young age (when breast tissue is undergoing rapid changes) and those who drank for long periods of time.
 - even moderate drinking (two drinks a day) can increase risk.



WEIGHT

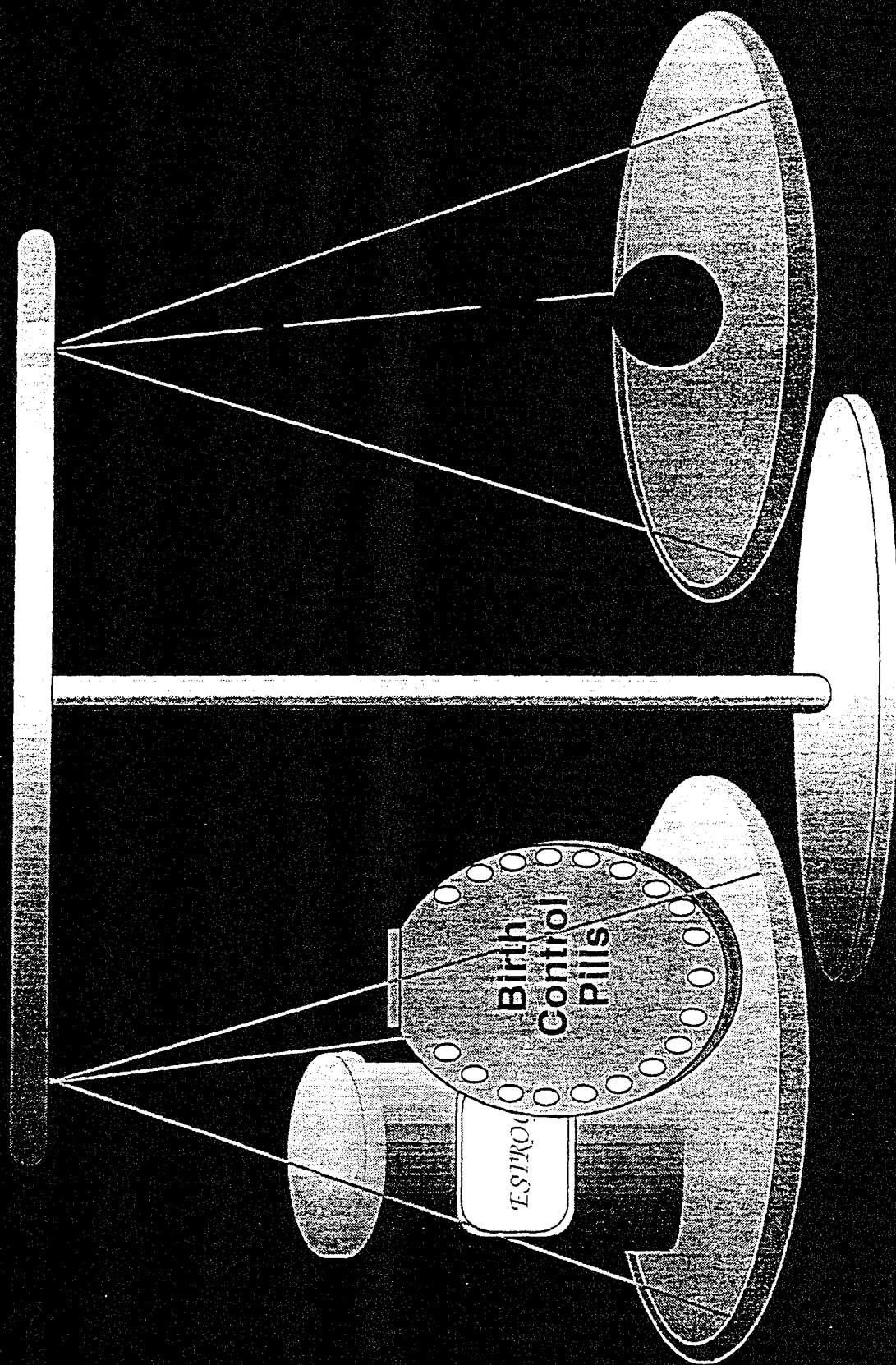


Estrogen is made with the help of enzymes in fat cells.

Weight

- Overweight
 - Being overweight after menopause does increase a woman's risk for breast cancer.
 - Estrogen is made with the help of enzymes in fat cells. After menopause, excess fat causes the continuation of estrogen production. It may be the continued circulation of estrogen that plays a role in breast cancer development.
 - Being overweight before menopause does not increase breast cancer risk.

Hormone Use



Hormone Use

The question of risk being associated with hormone use depends on when the hormones were used, for how long, and the doses involved.

- Oral Contraceptives

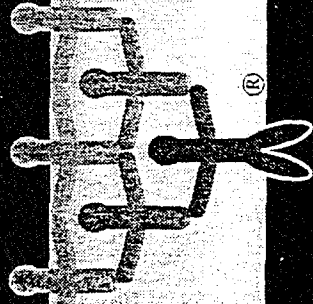
- Several studies have looked at the use of birth control pills and risk.
- Most studies conclude that there is no risk for most women.
- Some studies have found that women who started to use birth control pills at a very early age (before 20) and continued using them a long time do have a slightly increased risk.
- Oral contraceptives can decrease a woman's risk for ovarian cancer. If there is ovarian cancer in your family, may want to discuss this with your doctor.
- At this time, there is not enough proof to suggest women change their birth control methods.

- Hormone Replacement Therapy

- Moderate use of estrogen replacement for menopausal symptoms does not affect a woman's risk.
- High-strength preparations used in the past are associated with a slightly increased risk if they were taken for several years (15 or more).
- Trend since the early 1980s is to use lower-strength preparations
- There are several benefits to hormone replacement therapy: relieving symptoms of menopause, protection against osteoporosis, and protection against heart disease.

Exercise

- A recent study found that women who exercised a lot in their premenopausal years had lower rates of breast cancer.
- Women who showed a reduced breast cancer risk exercised at least 3.8 hours a week.

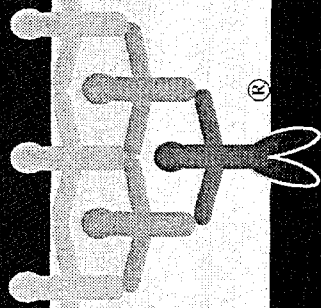


Recommendations

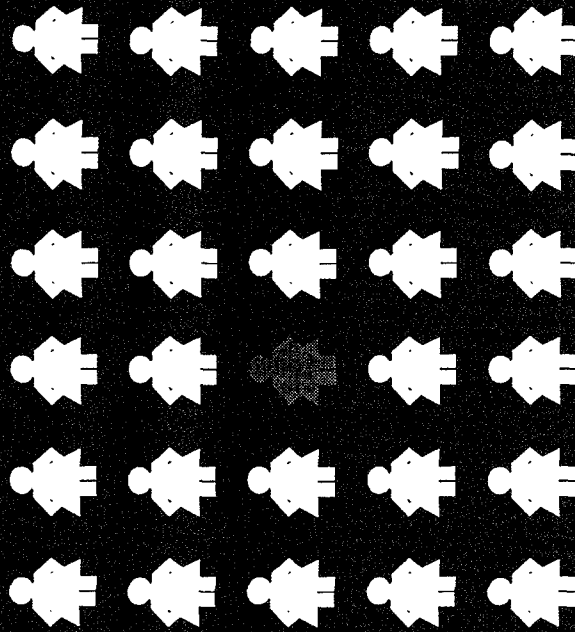
- Reduce dietary fat
- Maintain ideal body weight
- Eat more fruits & vegetables
- Consume little or no alcohol
- Exercise regularly
- Discuss hormone use with your doctor

Recommendations

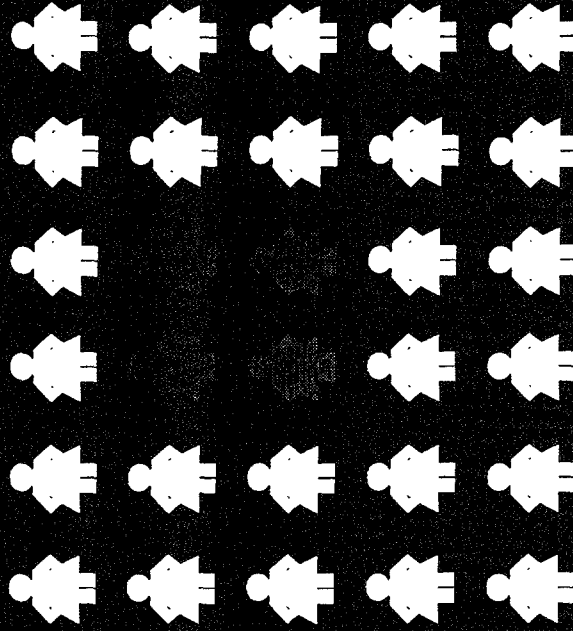
- Reduce Dietary Fat
 - Although the evidence that lower fat diets will reduce breast cancer risk is inconclusive, we do know high fat diets can increase risk of colon cancer and heart disease. Also low fat diets make it easier to reach and maintain an ideal body weight.
- Maintain ideal body weight
 - We are not certain that losing excess weight will reduce breast cancer risk in postmenopausal women, but we do know that being overweight increases your risk for several diseases, including heart disease--the number one killer of postmenopausal women.
- Eat more fruits & vegetables
 - Good advice for every one. Try to get at least five servings a day.
- Consume little or no alcohol
 - Occasional alcohol is not thought to increase your risk.
- Exercise regularly
 - We are not sure if this can decrease your breast cancer risk, but it has several other benefits.
 - Weight control, stress reducer, lowers risk of cardiovascular disease, high blood pressure and diabetes.
- Discuss hormone use with your doctor
 - The benefits outweigh any risk in most women, but discuss your personal situation with your physician.



Family History



No family history
1 in 30

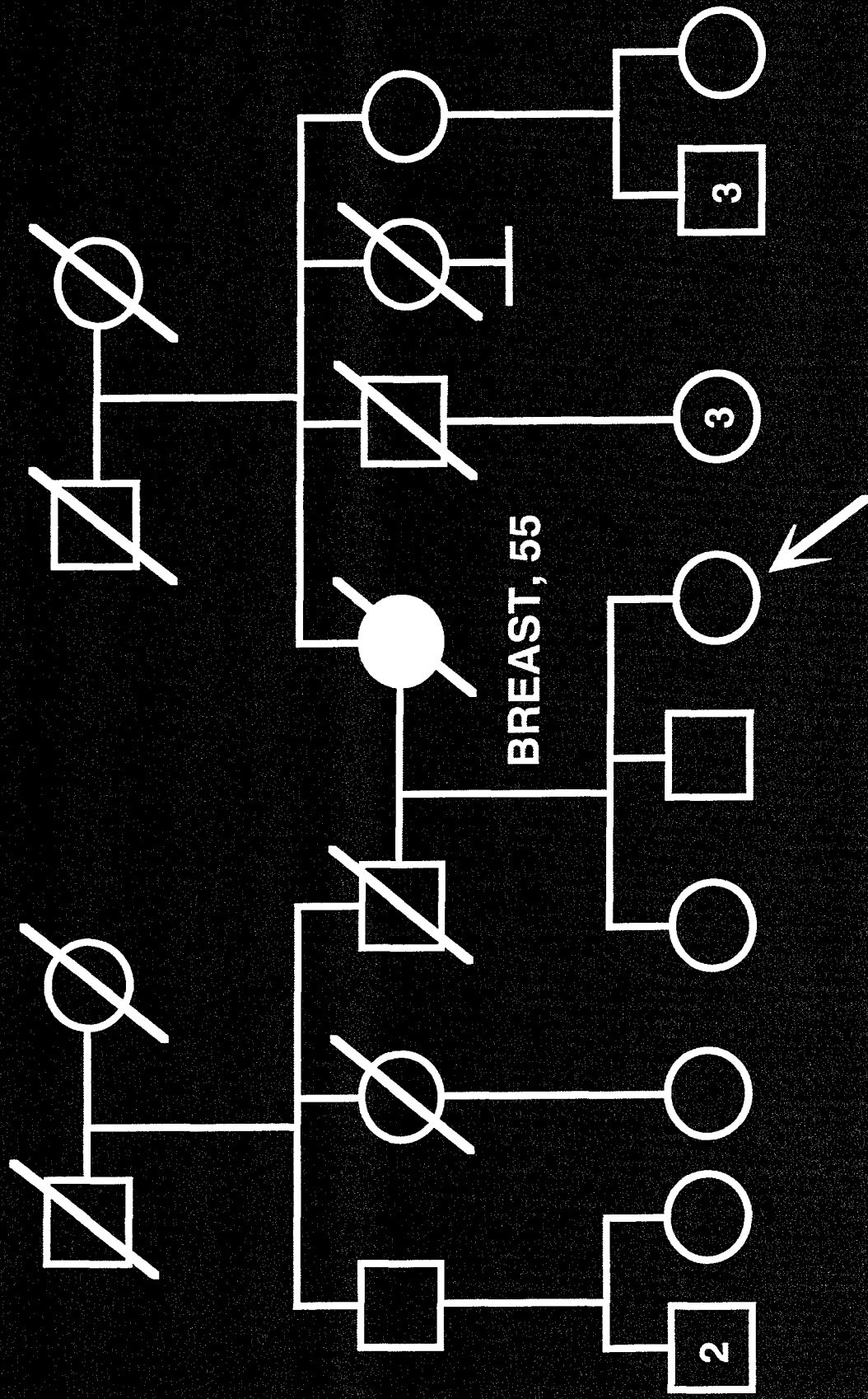


1 first degree relative
4 in 30

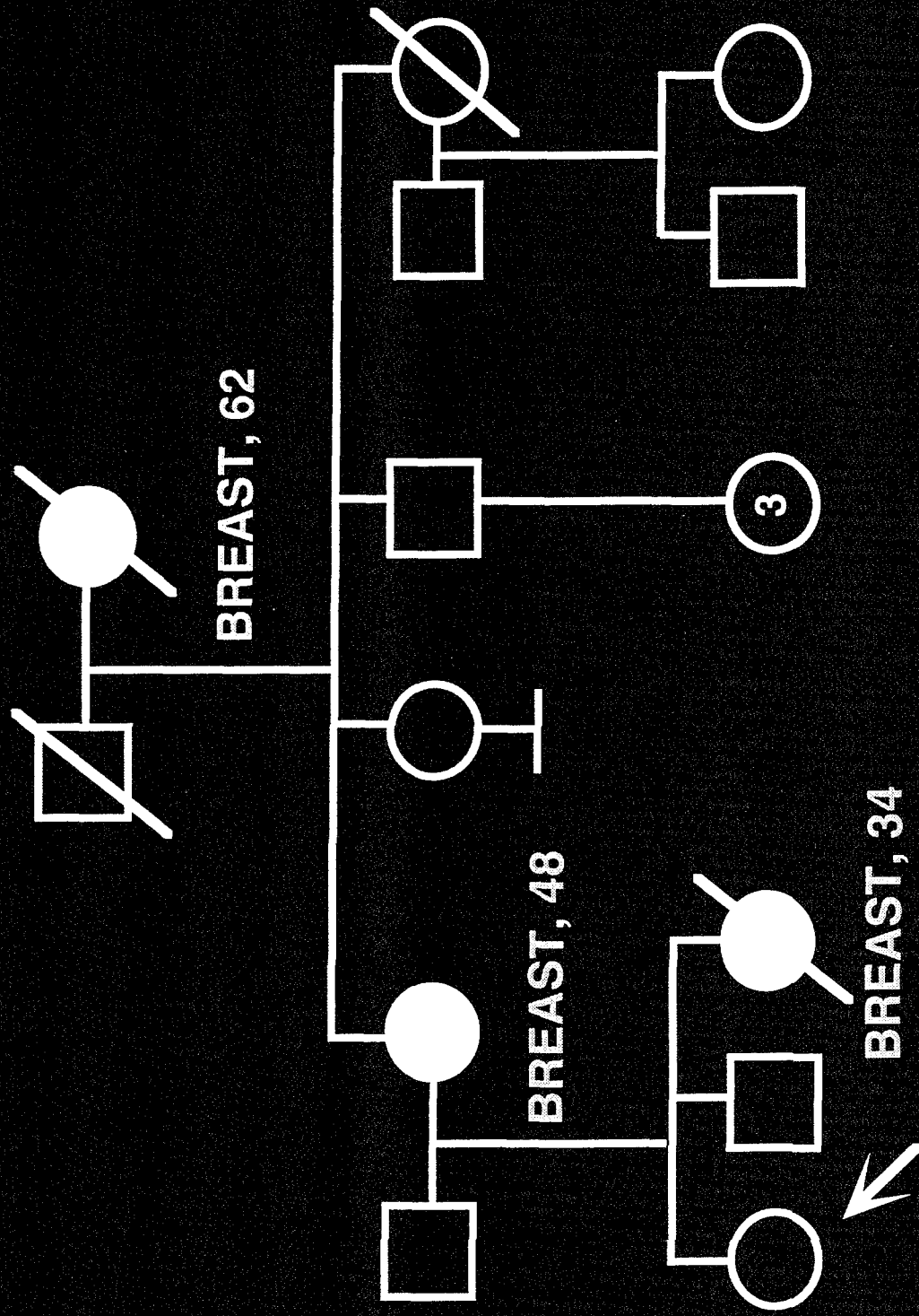
Family History

- Family history is an important risk factor for breast cancer.
 - This picture shows that if you had a group of thirty women with no family history of breast cancer, you would expect one of the 30 to develop breast cancer in a given year.
 - If all the women had one first degree relative(mother, sister, daughter) with breast cancer, you would expect 4 of the 30 to develop breast cancer.
- We are not entirely sure about the role of family history.
 - It could be because of a shared environment, such as having a similar diet.
 - We know that in some families, heredity is playing a role.
 - We believe that about 5-10% of breast cancer cases are due to women inheriting a damaged, or mutated gene from one of her parents.
 - The next several pages describe how this happens.

Pedigree: Sporadic Breast Cancer



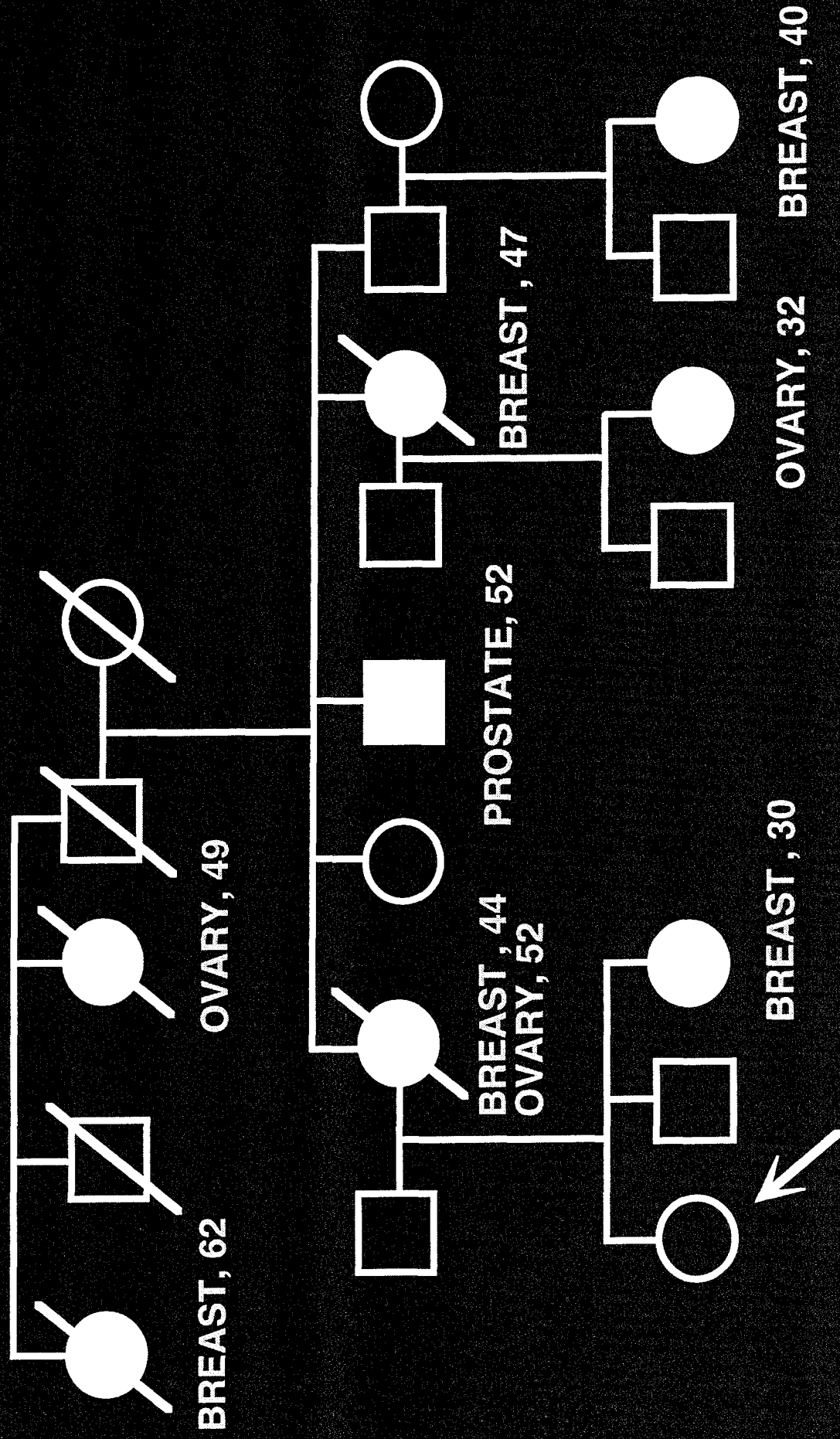
Pedigree: Hereditary Breast Cancer



Pedigree, Hereditary Breast Cancer

- The cancers in this family pedigree appears to be hereditary.
- There are several members of the family diagnosed with cancer.
- The cancers appears in members of different generations.
- Many of the cancers occur at young ages.
- It appears as though a mutated gene has been passed down form one generation to the next.
- Important note: the mutated gene can be passed down through both men and women.

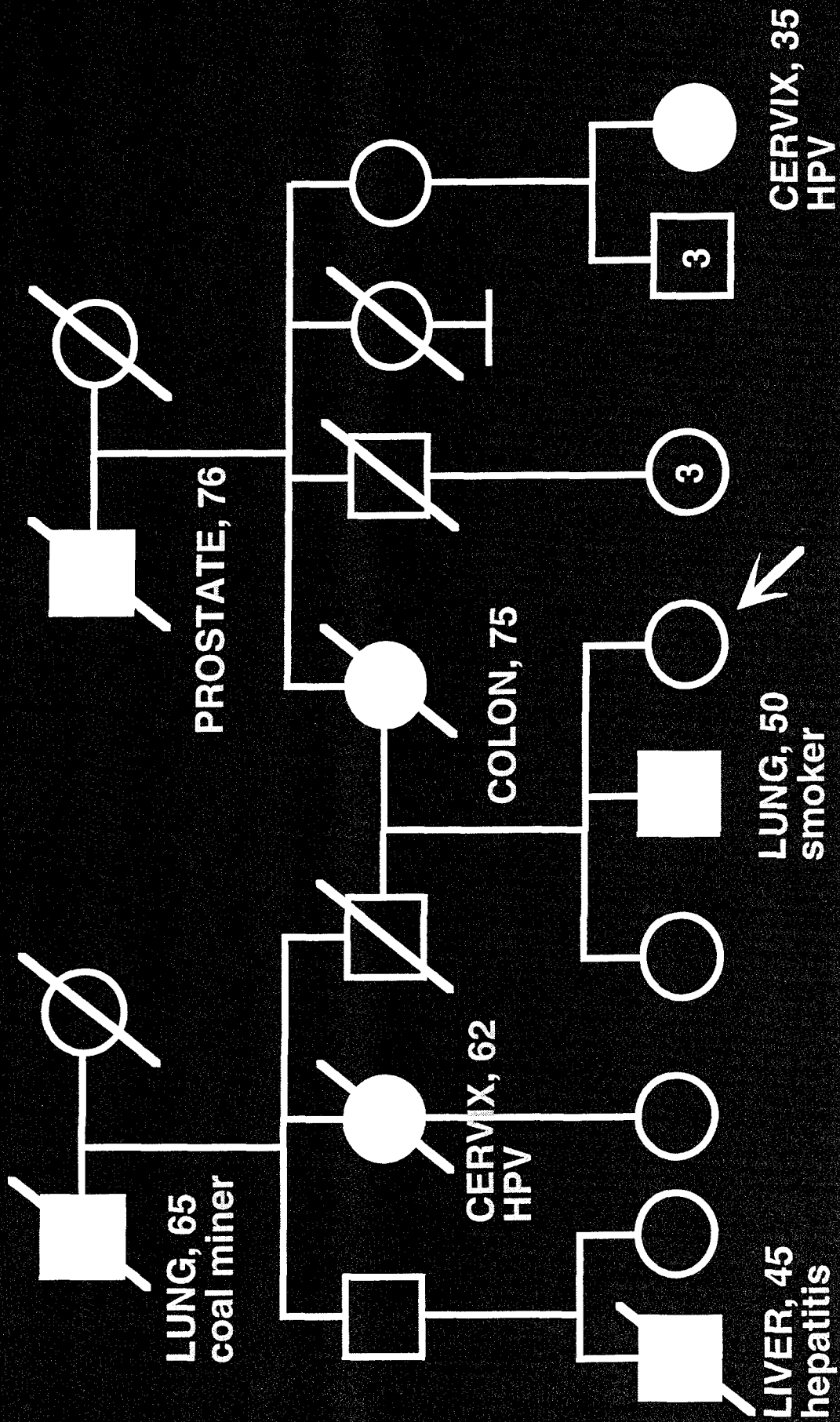
Pedigree: Hereditary Breast/Ovarian Cancer



Pedigree, Hereditary Breast, Ovarian

- The cancers in this family pedigree appears to be hereditary.
 - Notice that both breast and ovarian cancers occur.
 - Some of the cancers occur at early ages, and in different generations of the family.
- This pedigree fits what we call the Breast/Ovarian Cancer Family syndrome.
 - The cancer in this family appears to be caused by a mutation in a gene that has recently been identified. It is called the BRCA1 gene.
 - Researchers are currently working to develop a blood test that will tell a woman if she is carrying a mutated form of this gene.
 - A woman carrying a BRCA1 mutation is at very high risk for both breast and ovarian cancer.
 - Some of you may be eligible to have this test, or other cancer genetic tests. We will talk more about that, later.
 - There are other cancer syndromes that have been identified that include cancers other than breast and ovarian cancer.

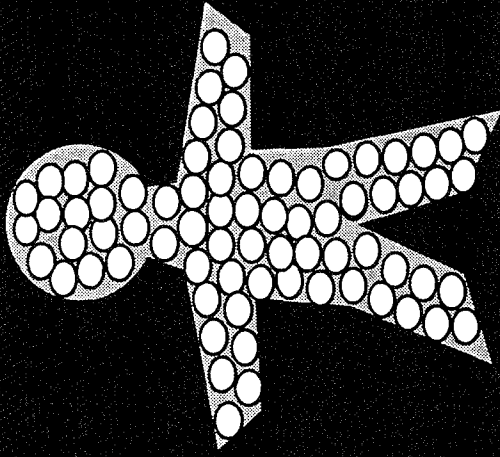
Pedigree: Familial family history of cancer



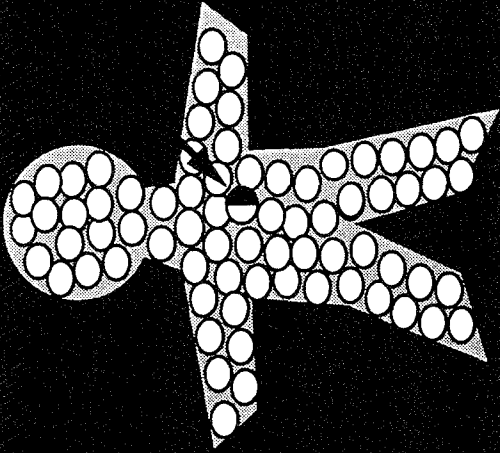
Pedigree, Familial

- The cancers in this family appears to be familial.
- That means there appears to be a hereditary pattern because there are so many cancers, however, it does not fit any of the patterns of hereditary cancers that we know of.
- May be hereditary, or may be due to other factors that we have yet to identify.

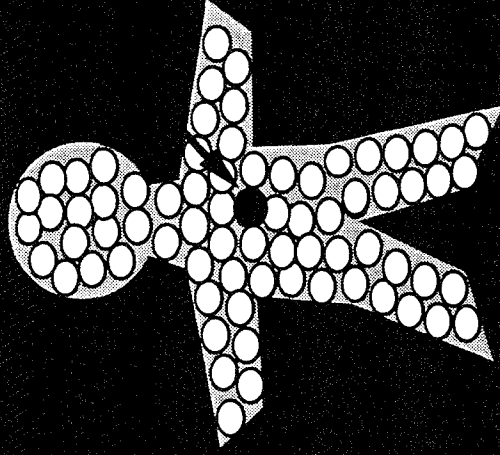
Sporadic vs. Hereditary



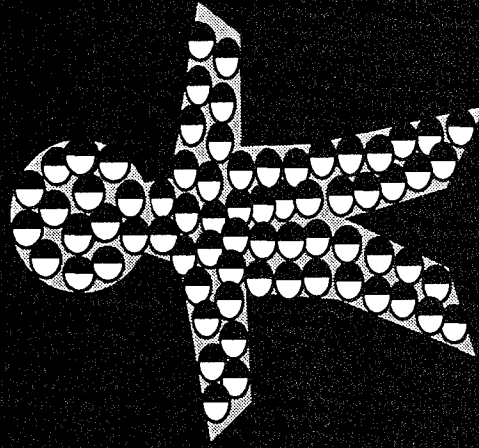
all cells have 2 normal
copies of the gene



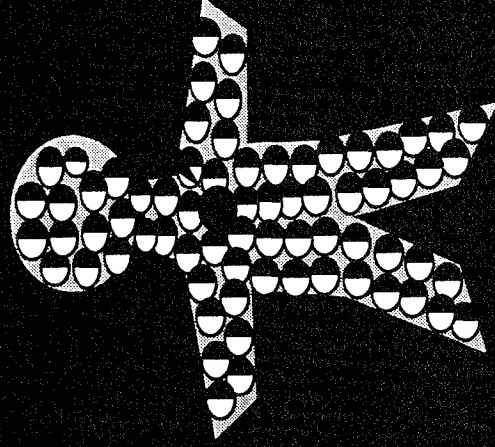
1st hit—one copy
is damaged



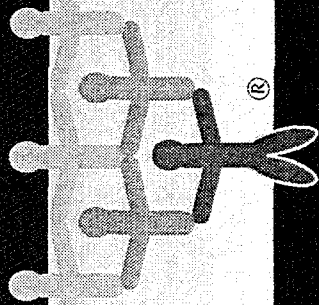
2nd hit = cancer



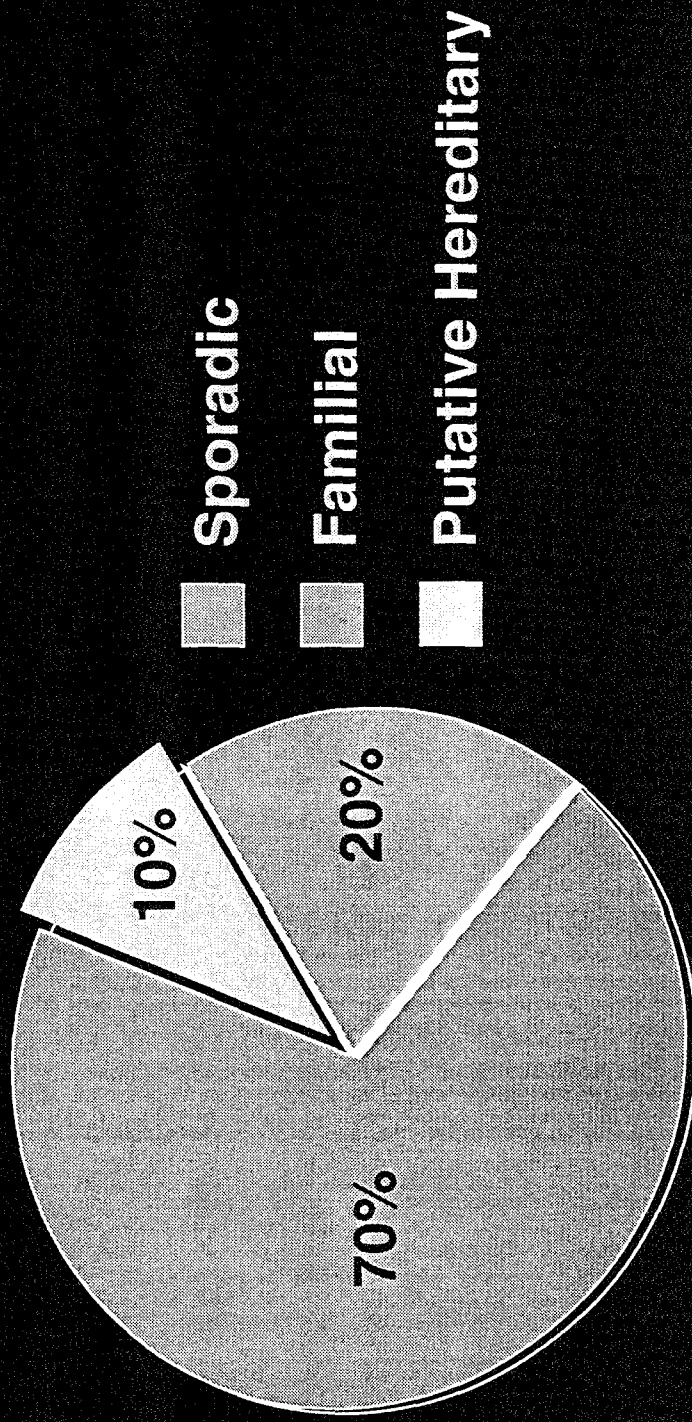
all cells have one damaged
copy at birth (1st hit)

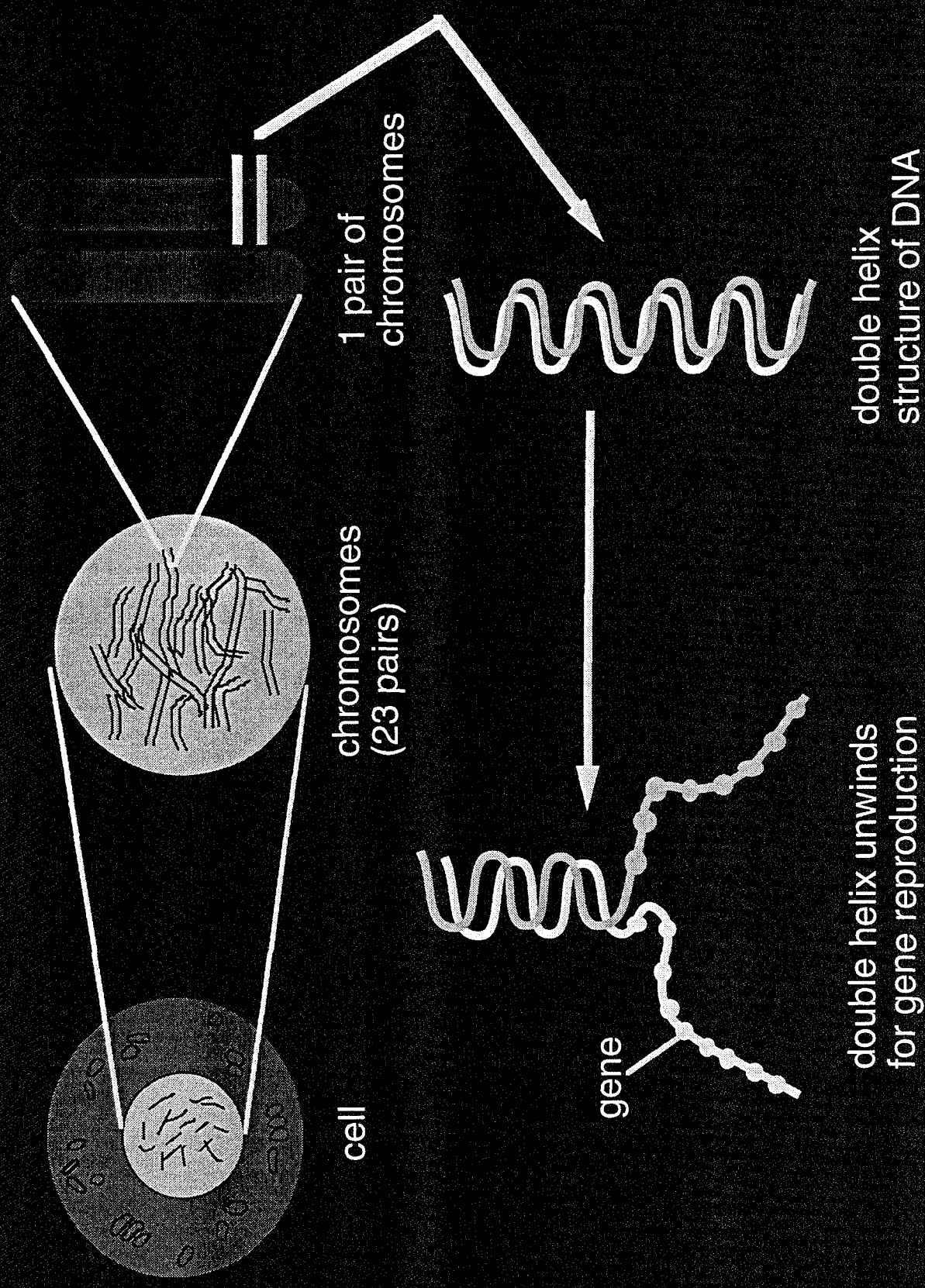


2nd hit = cancer

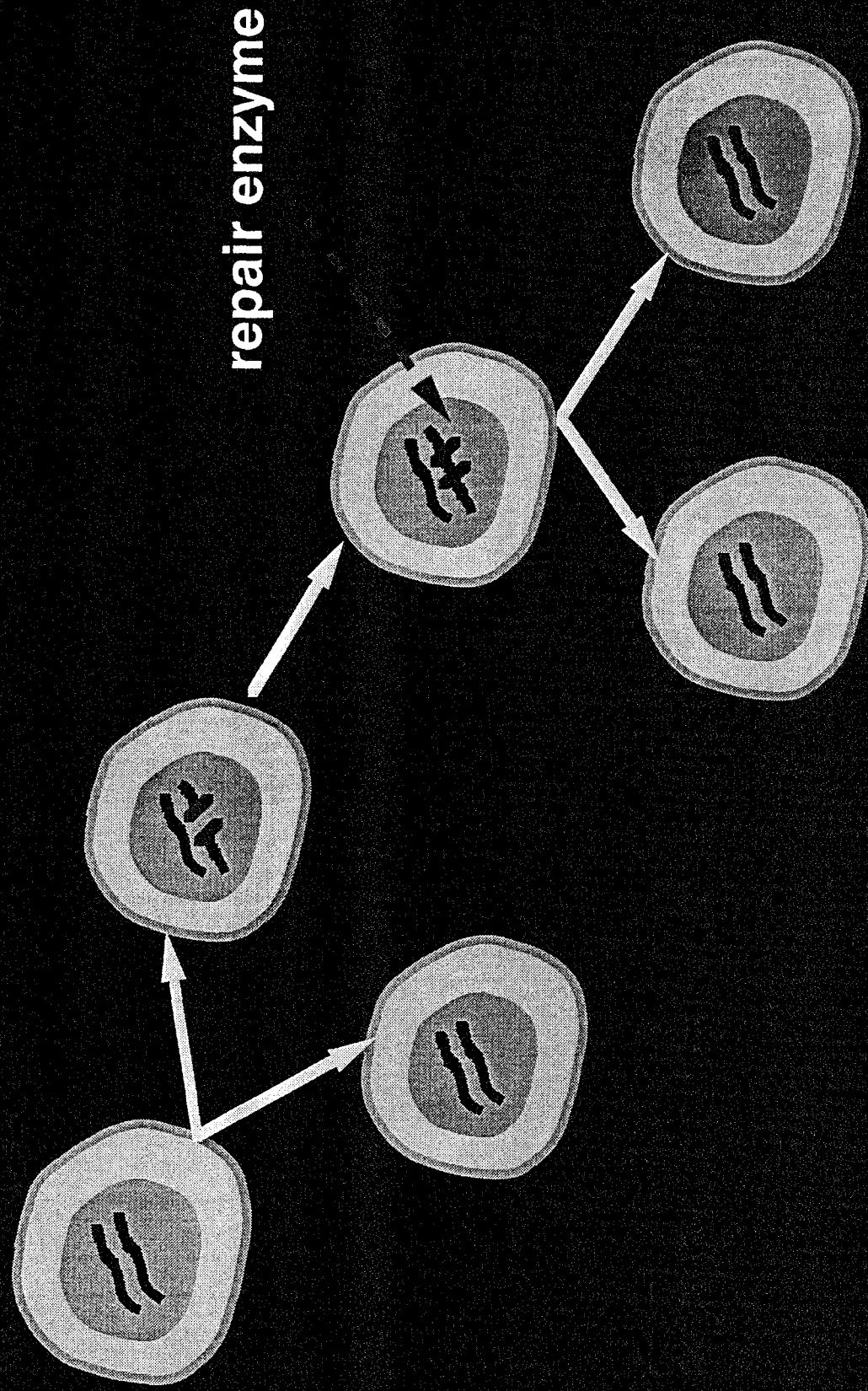


Familial Cancer Patterns

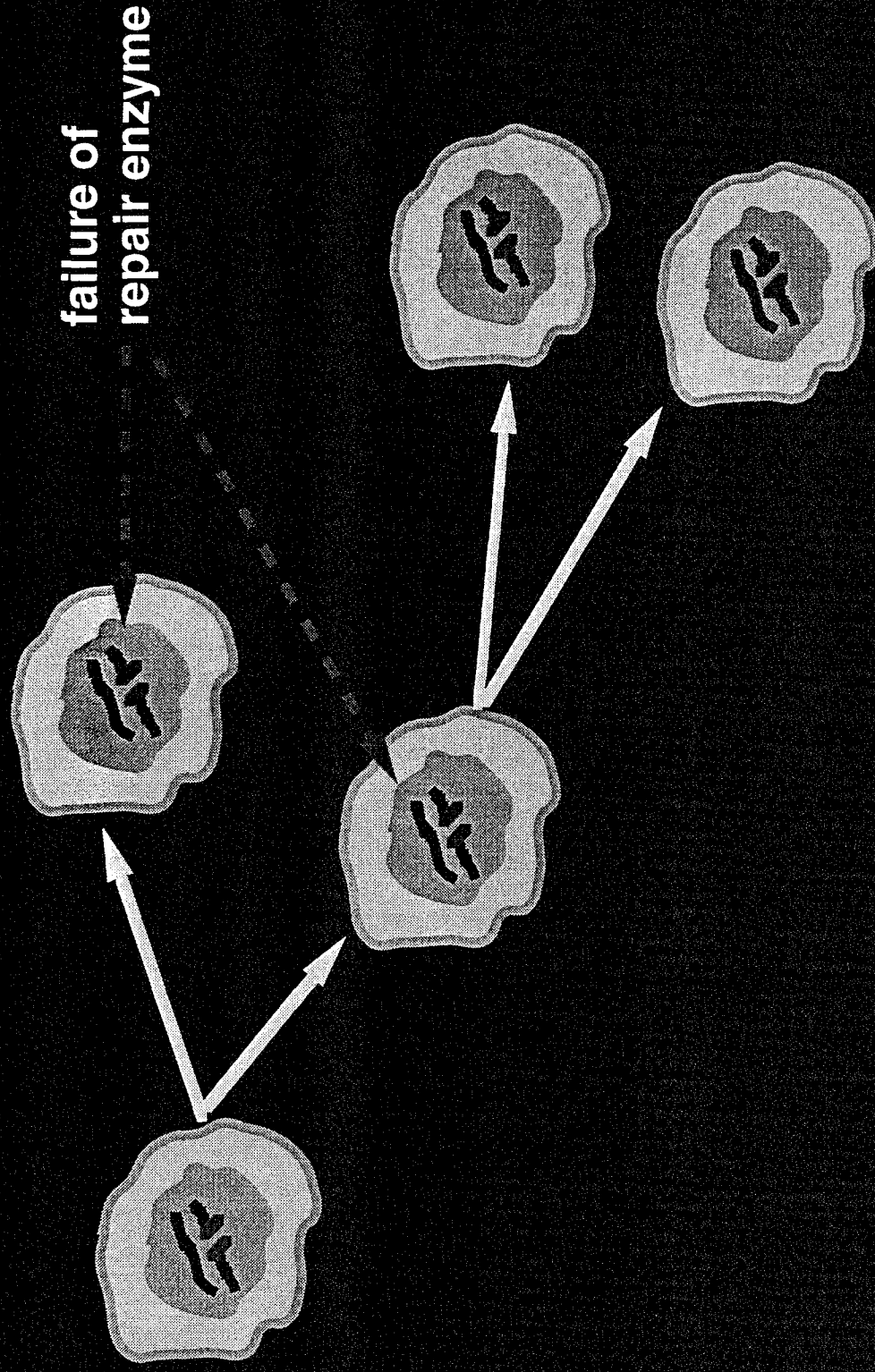




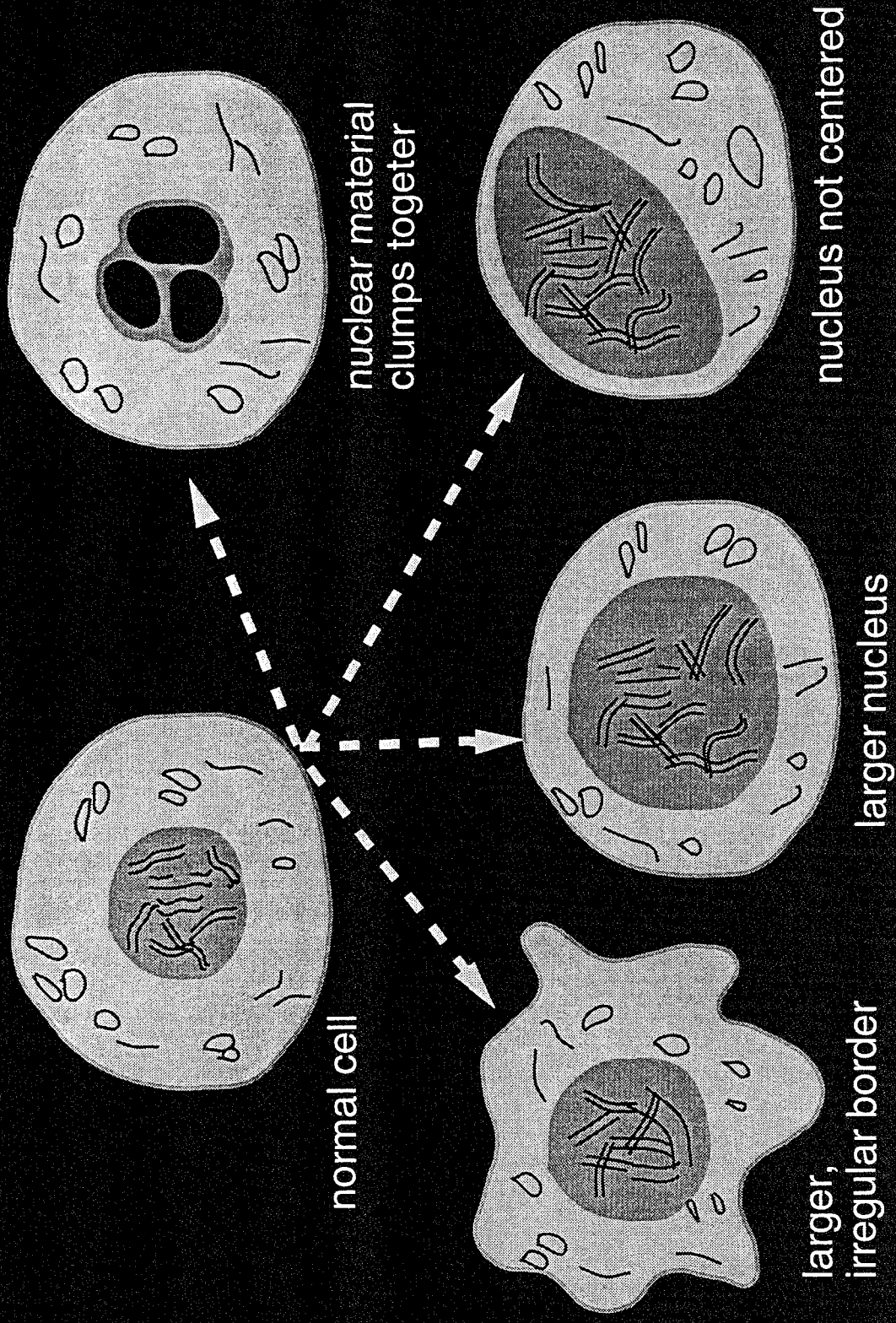
Cellular Genetic Errors



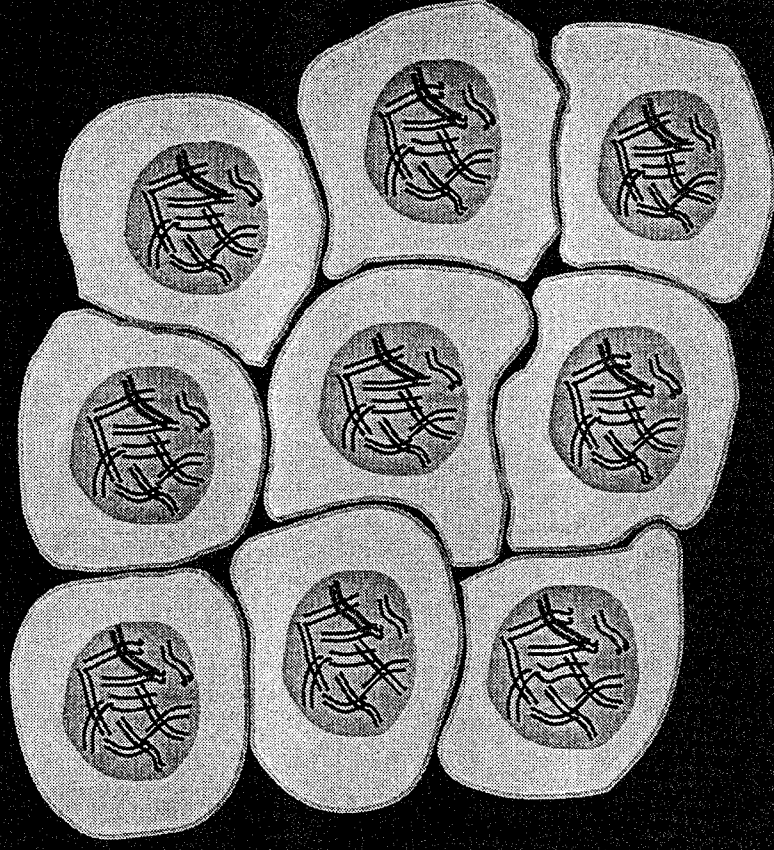
Cellular Genetic Errors (continued)



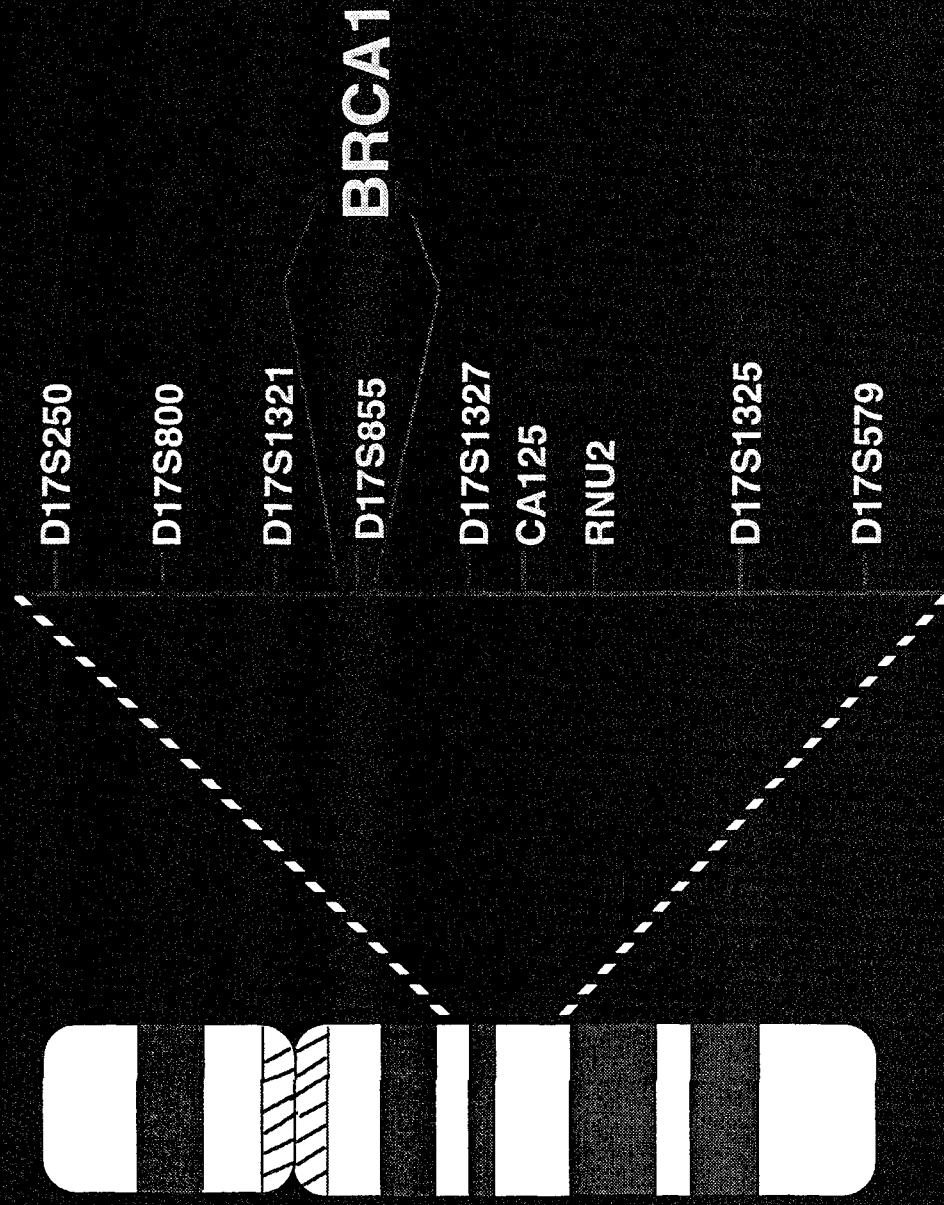
Examples of Genetic Defects



Accumulation of Abnormal Cells



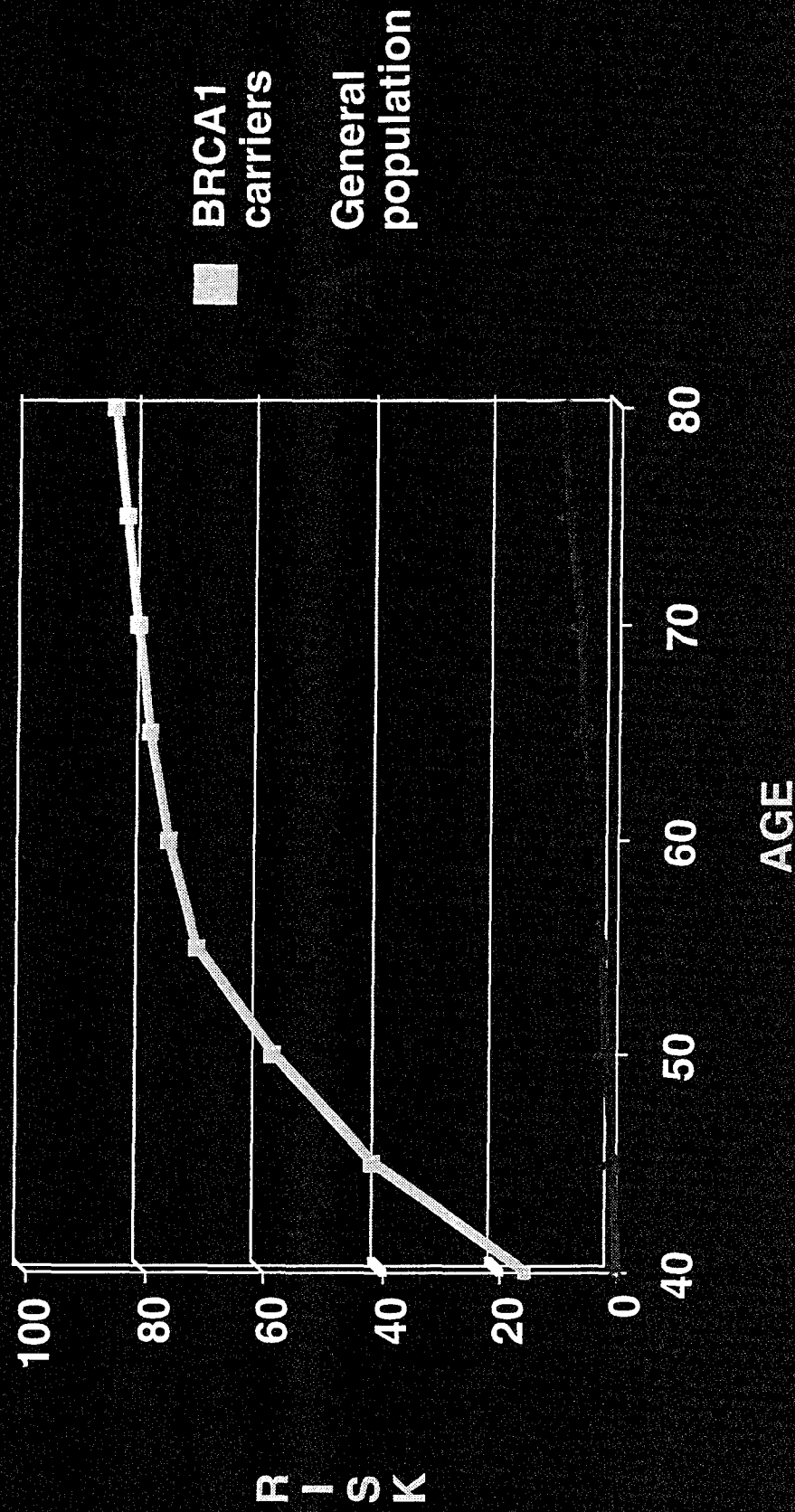
Chromosome 17



Chromosome 17

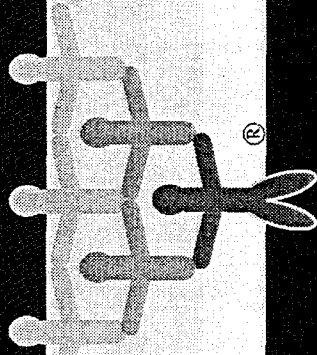
- The BRCA1 gene already mentioned is located on chromosome 17.
- Until the discovery of BRCA1 in 1994, we knew its general location on chromosome 17. We now know the exact location.
 - This makes a blood test for BRCA1 possible.
 - However, the BRCA1 gene is very long and mutations can occur in many different areas on the gene.
 - Scientists have found several of these areas and continue to look for more.
 - Once the majority of mutations are found, the testing for BRCA1 will become more widely available.
 - Currently, the testing is done predominantly through research studies, such as our program.

Cumulative risk of breast cancer in BRCA1 carriers vs. the general population



Cumulative Risk of BRCA1

- This graph shows the breast cancer risk of women who are BRCA1 carriers.
- Carriers refers to people who carry the mutated copy of BRCA1.
- A woman carrying BRCA1 has an 85% probability of developing breast cancer by the age of 80.
- Compare this to the general population where the risk to age 80 is only about 10%.
- We are not sure what the risk of ovarian cancer is, but the best estimate is about 40%.



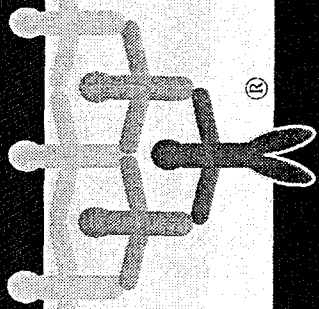
Benefits of Genetic Testing

- **Reassurance**
- **More accurate picture of risk**
- **Decision making**
- **More personalized screening recommendations**
- **Learn about your children's risk**
- **Help future generations**

Benefits of Genetic Testing

There are both risks and benefits of genetic testing for cancer. The benefits include:

- Reassurance
- Many women may fear they are carrying the gene but learn through the genetic test that they are not.
- More accurate picture of risk
- Decision making
- More personalized screening recommendations can be made.
- Learn about your children's risk.
- Help future generations.

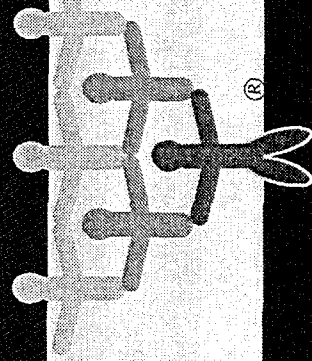


Limitations of Genetic Testing

- **Discrimination**
- **Emotional reactions**
- **Loss of privacy**
- **Does not eliminate other causes**
- **Concern about your children**

Limitations of Genetic Testing

- Discrimination
 - It is important that individuals who test positive for BRCA1 are not discriminated against in health and life insurance and employment issues.
- Emotional reactions
 - Individuals must anticipate what their reactions will be if they test positive or negative.
 - Family members may get different results, how will that affect relationships?
 - How will the results affect relationships with spouses or partners?
- Loss of privacy
 - It may be difficult for a person to keep the results from her family, even if that is what she prefers to do.
- Does not eliminate other causes of cancer
 - Even if you test negative, you may still be carrying another gene for breast cancer that has yet to be identified.
 - Risk never goes down to zero, it is always at least the same as the general population because you are also susceptible to environmental causes of cancer.
- Concern about your children.
 - If you test positive you may become anxious about your children. Most researchers agree that testing children for a disease that won't occur until later in life is not appropriate.
- Important note: as with any genetic test, the BRCA1 genetic test does have its limitations. These limitations will be discussed in detail with anyone considering the test.



Putting it into Perspective

Leading causes of death, females, 1990

| | |
|-------------------------------|---------------|
| Heart Disease | 359,270 |
| Cancer (except breast) | 193,648 |
| Cerebrovascular Diseases | 87,391 |
| Breast Cancer | 43,391 |
| Pneumonia, Influenza | 42,615 |
| Chronic Obstructive Lung Dis. | 37,263 |

Putting Risk into Perspective

- Comparing breast cancer to other causes of death
 - Heart disease is the leading cause of death
 - One in two women will die of heart disease in their lifetime.
 - One in nine women will develop breast cancer
 - Other cancers are the second leading cause of death after heart disease
 - And stroke and other cerebrovascular diseases are more frequent than breast cancer
- It is normal to have heightened awareness of breast cancer
 - When you have experienced a particular disease, or have a family history [lead in for next slide - breast cancer epidemic]

Breast Cancer Epidemic

- **Media Attention**

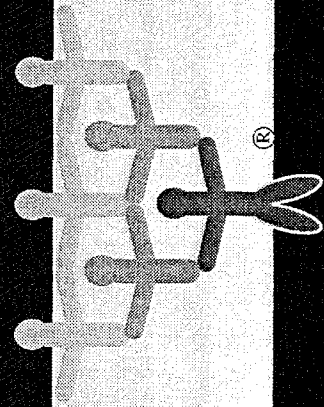
- There has been more media attention given to breast cancer over the past few years.
- This picture from Life magazine features women with breast cancer -some well know women:

Shirley Temple Black

Linda Ellerby

Marcia Wallace (the secretary on the Bob Newhart show)

- **Sub heading - Fighting Back ...what women are doing to help themselves**
 - more attention has been given to breast cancer because women are seeking more information
 - women are advocating for research and treatments to address breast cancer
 - your seeking information is a way of fighting back to help yourselves and your family



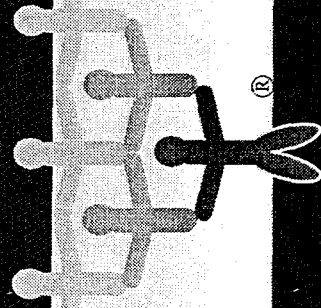
Early Detection

**The earlier breast cancer is found, the less
chance it has to spread...**

**...the easier the treatment
...the better the chance for cure.**

Early Detection

- One way to fight back is to find cancer early
- Goal of early detection
 - to detect and treat breast cancer at its earliest stages
 - has less chance to spread
 - easier to treat
 - and has better chance for cure
- Early Detection has helped
 - We are still learning how measures such as diet and other chemoprevention efforts like Tamoxifen may prevent breast cancer
 - But we know that early detection with effective treatments can make a difference
 - Over a 16 year period (1973 to 1989) there was about a 28% increase in the number of new cases of breast cancer; that increase has now leveled off.
 - But most of those cancers were earlier stage and the number of deaths for the same period went up only 1%. (Helszlouer, 1995)



3 Steps for Early Detection

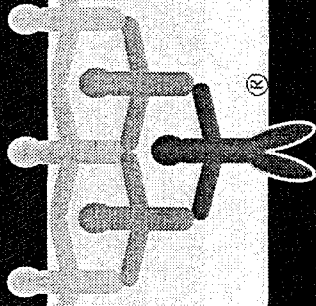
Step 1 Regular mammograms

Step 2 Annual clinical breast exam

Step 3 Monthly breast self exam

3 Steps for Early Detection

- Regular Mammograms
 - recommendations are for all women to be routinely screened after age 50
 - recommendations for women who are in high risk groups will vary based on
 - family history
 - their age
 - the clarity of their mammogram
- Annual Breast Exam
 - by a physician or health professional
- Monthly breast self-exam



Mammogram

- Early breast cancer has no symptoms
- Can detect cancers 18-24 months before you or your doctor can feel them
- 90% of these small cancers are curable

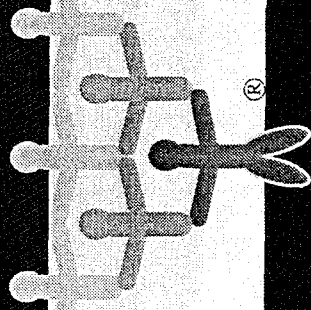
Mammogram

- Purpose of mammograms
 - to find disease when it is so small that it has no symptoms
 - most breast lumps can be felt about the size of a pea
 - mammograms can detect about size of pinhead
 - this is usually about 2 years before they can be felt
 - these are early cancers that are easy to treat and cure
- Caution
 - there is no screening test that is perfect
 - mammograms can miss about 10% of cancers
 - may be due to density of breast tissue-- especially in younger women
 - The glandular material shows up white on mammograms; so do abnormalities.
 - Very dense breast tissue makes a mammogram more difficult to read. Because of this, and because breast cancer is not common in younger women, mammograms are generally not recommended in young women. However, in young women with a family history of breast cancer, screening may begin at an early age. It depends on the individual's risk and the clarity of her mammograms.
 - These glands shrink with age--making a mammogram easier to read.

Pictures of mammograms

- Premenopausal
 - more density
 - glandular tissue shows up white
- Postmenopausal
 - there is decrease in glandular tissue
 - fatty tissue and connective tissue show up gray
 - better contrast to detect changes in breast tissue
- Microcalcifications
 - can appear as pinpoint specks on mammogram
 - can be normally present
 - clustering in one area may be suspicious pattern

[Ultrasound - is used as a diagnostic tool to identify if an area is solid or fluid filled and is not routinely used for screening.]

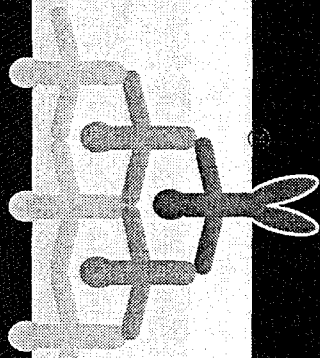


Clinical Breast Examination

- **By a doctor, nurse, or other health professional**
- **During a routine check-up or Pap test**

Clinical Breast Exam

- Mammograms can miss a small percent of lumps
- Rely on several screening methods
- Done by doctor or nurse at routine check-up or GYN visit checks breasts and under your arms for lumps
- Trained physicians, nurses and physician assistants have high rate of detection (87%) of lumps about the size of pea (about 1 cm)



Breast Self Examination

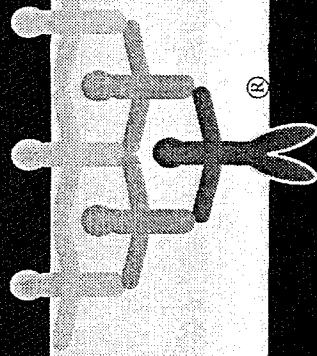
CHECK FOR:

- Lumps
- Dimpling
- Scaling
- Puckering of the skin
- Discharge from the nipple

Breast Self-Exam

Two parts to every good breast exam

- Visual Inspection
 - Looking at your breast in the mirror
- Examining your breasts
When doing visual inspection you check for:
 - Lumps
 - Dimpling or flattening
 - Scaling especially around nipple
 - Puckering of skin
 - Discharge from the nipple
 - Any change in skin texture (like orange peel skin)



Prevention Options

- **Changes in Lifestyle**
- **Chemoprevention**
- **Prophylactic Surgery**

Prevention Options

- Changes in Lifestyle

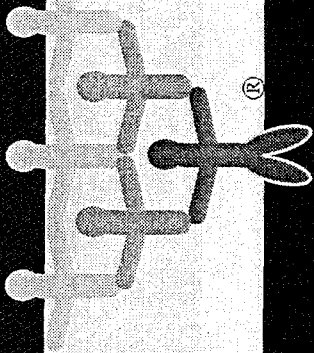
- Diet
- Exercise
- While we can't guarantee that changes in lifestyle will reduce breast cancer risk, we do know that a good diet and exercise program can reduce your risk of other chronic diseases.
- We hope our study will lead to more information on reducing risk in the future.

- Chemoprevention

- Tamoxifen Trial: Tamoxifen is a drug that has been used for several years by women who have had breast cancer. Tamoxifen reduces the risk of a recurrence of breast cancer in these women.
- We are currently studying whether Tamoxifen can prevent breast cancer from occurring in women who have never had breast cancer.
- The study is being conducted in over a hundred hospitals in the U.S. and Canada, and Fox Chase and all the Fox Chase Network hospitals are participating. If you would like more information about the study, please let me know at the end of this session.

- Prophylactic Surgery

- Bilateral mastectomy
- CAUTION: There is a lack of studies on the effectiveness of P.M. It is difficult to remove 100% of the breast tissue and there have been a few cases of women being diagnosed with breast cancer years after the surgery. While it does reduce risk significantly, we can't say it is 100% effective.

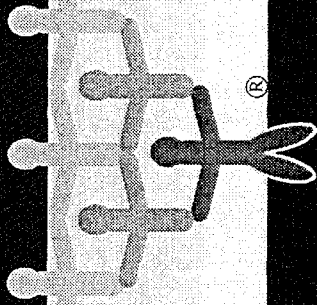


Program Options

- Screening
- Clinical exams
- Genetic counseling
- Genetic testing
- Other research

Program Options

- Screening
- Genetic Counseling
- Genetic testing
- Other research

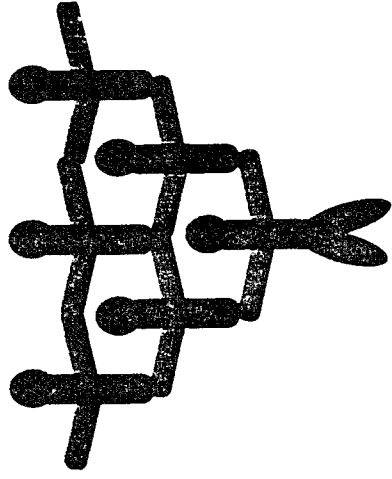


Summary

- Normal anatomy & breast function
- Risk factors
- Family history & genetics
- Screening
- Prevention

APPENDIX H

1997



What your
family history
can tell you
about cancer.

FCCC

Participant ID # _____

FRAP-____,____
Participant Contact Log
Baseline Survey

Name :

Address :

Sample

Telephone Number :

Best time to call:

Date of Birth :

Patient's Name :

Relationship to patient :

Date letter sent :

| Date | Time of Attempt | Time of Completion | Disposition | Initials |
|-------|--------------------|-----------------------|-------------|----------|
| _____ | _____ | _____ | _____ | _____ |
| _____ | _____ | _____ | _____ | _____ |
| _____ | _____ | _____ | _____ | _____ |
| _____ | _____ | _____ | _____ | _____ |
| _____ | _____ | _____ | _____ | _____ |

Comments

High Risk Registry Program

Telephone Script

Hello. My name is _____ and I'm calling from the
<Network Hospital> High Risk Registry Program for relatives of women with
(breast/ovarian) cancer.

*Case 1: Because you have a family member with breast cancer, you have recently requested
information about your risk of developing cancer...*

*Case 2: Your name has been given to us by _____. (He/She/They)
thought you may be interested in our program because of your family history-of cancer.*

*Case 3: Your physician has recently recommended that we contact you because of your family
history of breast cancer... (optional: because of your personal history of breast cancer).*

Do you have a few minutes to talk with me now about our program?

If not convenient...

-- arrange to call back

*-- if woman is definitely not interested in discussing the program, thank her for her time and
terminate the call (probe for reasons, check below).*

If no, thank woman for her time and terminate the call...(explore and check response)

- _____ No Time
- _____ Lives too far away
- _____ Doesn't think it's important for her
- _____ Concerned about cost
- _____ Doesn't want to talk about cancer
- _____ Doesn't feel at increased risk
- _____ Can't come to FCCC
- _____ Is being screened regularly
- _____ Family wouldn't approve
- _____ Other _____

If yes, continue...

First of all, can you tell me a little bit about your family history of cancer, and then I'll explain our program to you and you can tell me whether or not it's something you would be interested in.

Family History: _____

*1) (if woman has no family history of cancer, tell her the program is designed for women with a family history of cancer and would probably not be appropriate for her). **Probe for concerns...** Refer to appropriate source.*

2) If woman has personal history of breast cancer, tell her the program is for her relatives who do not have cancer, but there would be important information for her as well.

3) If has appropriate family history, continue...

Now I'll explain our program to you.

Our program is designed to help give women like yourself information about their risk for (breast/ovarian) cancer based on their family history in addition to information about any other cancers which might have a family association. The program consists of a one and a half to two hour group educational session with a health professional from the Fox Chase Network. The group educational session will go over breast cancer and what it means to you because of your family history, the risk factors associated with breast cancer, as well as important information on issues such as diet, birth control and hormone replacement therapy, smoking and alcohol. If you have concerns regarding preventive surgery, this can also be addressed. We'll also discuss what risk there may be in the future for other members of your family, such as your children.

We will provide the latest information regarding genetics and cancer. We will provide an overview of what we are looking for in families, the progress that is being made in this area and what this means to you and your family.

This session also involves an explanation of the various screening exams for breast cancer and other important cancers, and information on their accuracy. We will then recommend a series of screening exams that are the most appropriate for you based on your age and family history.

The educational session is <cost arrangement>. We just ask women to complete a questionnaire for research, and this questionnaire will help us to give you feedback about your risk for breast cancer. If you decide to come in, I will mail the questionnaire to you ahead of time and ask that you bring it in with you to your visit.

Following the educational session, there is the opportunity to:

- come into <Network hospital> and meet with one of our nurses trained in Familial Cancer Risk Assessment;
- receive your family pedigree, a family tree that looks at the cancer across several generations;
- get feedback about the family pattern of cancer and what it means for you.

This is not a requirement, however, and you can make this decision after you have attended the session.

Do you think you would be interested in participating in such a program?

- (1) _____ Yes (continue on next page)
- (2) _____ No (thank for time and close)
- (3) _____ Not Sure _____ (tell her you will keep her name and number and call her back in a month or two).

If yes...

That's wonderful. We can schedule an appointment now if you'd like.
(Schedule appointment).

Appointment date and time

Now, I'd like to collect some more information...

Name: _____

Address: _____

Home Tele. # (____) _____ Work Tele. # (____) _____

Date of Birth: _____

Referral Sources:

(1) _____ Self

(A) _____ Fact Sheet

(B) _____ Newspaper Article

(C) _____ Refused or Ineligible - Tamoxifen

(D) _____ Called FCCC and was referred

(E) _____ Other _____

(2) _____ Physician _____

(3) _____ Hospital _____

(4) _____ Patient _____

(5) _____ C.I.S. _____

(6) _____ Relative a participant _____

(7) _____ Friend a participant _____

(8) _____ A friend told her about program _____

(5) _____ Other _____

For Accruals Only

Gail Model Information:

_____ Age

_____ Age at Menarche

_____ # of Breast Biopsies

If yes, do you know the diagnosis? _____

_____ Age of First Pregnancy

_____ # of FDRs with Breast Cancer

Do you have any questions? You will be receiving the questionnaire within the next week. I will give you my telephone number in case you have any questions. It is <phone number>. Please try and come in a half an hour early for your appointment because we would like to go over the family history part of your questionnaire with you. I will be sending you a confirmation letter and directions to <Network hospital>. Feel free to call me with any questions. I will be talking to you soon. **Thanks again!**

Standard Letter to confirm Appointment for Education Session

<Network Staff>
<Network Address 1>
<Network Address 2>

<date>

<Name>
< Address 1>
<Address 2>

Dear Ms. :

I would like to confirm <DATE> at <TIME> as the date and for the Breast Cancer Risk Education session (*adapt name to individual Network Hospital*). If possible please try to arrive one half hour early to process the necessary paper work. Enclosed are directions to <Network Hospital> *Add any other instructions or directions for where you will meet..*

I have also enclosed a questionnaire for you to fill out. The Health History Questionnaire will provide us with more information about your personal health and family history of cancer. With information from this questionnaire we will be able to give to you

- a Family Pedigree - this is a type of family tree that looks at the history of cancer in several generations
- Feedback about your family history and your own personal risk for cancer.

All of the information provided on the questionnaire will be kept completely confidential. A code number will be used to track any information and your name will not be used. Please complete the questionnaire as best you can and bring it with you to the education session.

Should you have any questions, please call me <Network Staff> at <Network phone #>. Thank you very much.

Sincerely,

<Network staff Name>

HEALTH HISTORY INSTRUCTIONS

- I. Review entire HHQ for missing data while participant/patient is filling out the psychological measures.
- II. Section B. Review each page with participant/patient to fill in missing data. Pay particular attention to Alive, Deceased. Ask if any dates are estimates, if yes, circle.

Part 2: Ask if any siblings have a different parent than the participant. If yes, ask which is the common parent. If mother, write HM (for half sibling by mother) in the *"office use only"* column next to the appropriate siblings. Write HF for half siblings by the father.

Part 3: Ask if the children are all fathered by the spouse named in Part 1. If not, use lines 9 and 10 of Part 1 to fill in the names of the man or men who have fathered the children. Collect information on date of birth, cancer, etc., if available. Write the corresponding father's number in the *"office use only"* column for the appropriate child on Part 3.

Example: If children 17 and 18 are fathered by a man other than #8 on Part 1, fill in the father's name on line 9, Part 1. Write #9 in *"office use only"* for children 17 and 18 on Part 3.

Part 4: Ask if the participant's mother and her siblings have the same parents. If some are half siblings fill in HM for half by mother or HF for half by father in *"office use only"* column.

Part 5: Same as Part 4, but for father's siblings.

Part 6: If the participant lists additional relatives, ask how they are related to the participant. Write the number of the corresponding relative that connects the two in *"office use only"* column in Part 6.

Example: If #35 and #36 are cousins and related to the participant through her mother's sister #24, write 24 in the *"office use only"* column in Part 6. If #37 is a niece through participants brother #14, write 14 in the *"office use only"* column in Part 6.

- ** Use lines at bottom of page as needed. If the participant uses Part 6 for relatives that spill over from other sections (i.e., siblings, children, aunts or uncles), note on bottom of the corresponding page that these additional relatives are listed in Part 6. For example, if she has more siblings listed on Part 6, make a note of this on the bottom of Part 2.

<cbs/hlth/instruc>

Group Educational Session

Prior to Session:

- * Have ready:
 1. flip chart or slides for educational session
 2. Folders made up for each participant
 3. Pens or pencils
 4. Dorlands, if your Network Hospital has opted to send letter and screening recommendations to the participant's primary care provider.
- * Meet with women in <designate area> at <designated time>, preferably 15 to 30 minutes before session.
- * Collect and go over the Health History Questionnaire with each participant
- * Check for date of birth, half and full siblings, father #'s, additional relative information and missing data. (see Health History Instructions)
- * Write in dates of session on Health History Questionnaire (HHQ).
- * Make sure to collect the Health History Questionnaire and put into individual folders.
- * Bring woman to assigned room.

During the Session (if there is a second person to help):

- * Keep all "No shows" aside and mark on telephone survey. (call for new session)
- * Go through HHQ's to ensure all information is up to date.
- * Check the last page of HHQ for physician information. Look in Dorlands to complete address and telephone number if available.
- * Copy the physicians name, address, and telephone number on both the participants form (in participant's packet) and the physician letter (so individual letters can be done at the end)
- * On participant letter try to write the woman's age and date of last mammogram (time permitting). This will help to "quicken" the letter writing process at the end of the session.
- * Put patient packets aside so can be passed out at end of session.
- * For those network facilities using the Gail Model Scores, pass out sheets when facilitator is ready.

At The End Of The Session:

- * Have packets ready for distribution that would include:
 1. Interest checklist form - this form will ask about interest in
 - a. participating in an individualized risk assessment session
 - b. having a letter sent to their physician with recommendation for screening.
(*This form is signed by participant and serves as a consent to send a letter to their primary care providers.*)
 2. Sheet with <Network Staff> phone number to call for making appt. for individual risk assessment session.
 3. An Billing information <Billing decisions made by each Network Institution>
- * Give out packets to each individual.
- * Tell them that we would like to send a letter of recommendations to their physician. If they would like this done, please check yes and sign their name on Interest Sheet.
If they have not given physician's name, address and telephone number on HHQ, they can now write in their Doctor's name. (some may have already done this)
- * We will also mail them a letter of screening recommendation and enclose family pedigree.
- * Explain Individual Risk Assessment process.
 1. Give times that you are available to meet
 2. Explain that they will receive (at that Session)
 - a. pedigree expansion - will go over pedigree and expand the family information
 - b. preliminary information about the family pattern of cancer
 3. After the session - the pedigree information is reviewed by the FCCC Pedigree Review Committee here appropriate families are identified for genetic studies.
 4. Make sure that it is clear that genetic studies are not appropriate for everyone and that this is a process that can take weeks or months. Genetic studies are still research and not a diagnostic test
- * Tell them they can be involved with the High Risk Registry program in a variety of ways and there is no obligation.
 1. Some women come only to the education session and give their HHQ
 2. Some women will go one for the risk assessment but opt not to have genetic testing
 3. Some women have the risk assessment and the genetic testing.
- * If they would like to make an appointment they should contact <Network Staff> designated.

Following Session:

- * Complete letters to participants and physicians.
- * You will need to write in the physician's addresses for those who were incomplete.
- * The next day, HHQs need to be sent to Fox Chase Cancer Center for data entry and generation of family pedigree. (Count 3 week complete turn around time)
- * When pedigrees are returned, you are ready to do individualized risk assessment session.